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As filed with the Securities and Exchange Commission on September 25, 2017

Registration No. 333-220337

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 20549

AMENDMENT NO. 1 TO
FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

RHYTHM PHARMACEUTICALS, INC.

(Exact name of Registrant as specified in its charter)

Delaware
(State or Other Jurisdiction of
Incorporation or Organization)

2834
(Primary Standard Industrial
Classification Code Number)

46-2159271
(I.R.S. Employer
Identification Number)

500 Boylston Street
11th Floor
Boston, MA 02116
(857) 264-4280

(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

Keith M. Gottesdiener, M.D.
Chief Executive Officer and President
Rhythm Pharmaceuticals, Inc.
500 Boylston Street
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Boston, MA 02116
(857) 264-4280

(Name, address, including zip code, and telephone number, including area code, of agent for service)

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**Approximate date of commencement of the proposed sale to the public:
As soon as practicable after the effective date of this Registration Statement.**

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer" "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer o

Accelerated filer o

Non-accelerated filer
(Do not check if a
smaller reporting company)

Smaller reporting company o
Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. o

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Proposed Maximum Aggregate Offering Price⁽¹⁾	Amount of Registration Fee⁽²⁾
Common Stock, \$0.001 par value per share	\$115,000,000	\$13,328.50

(1) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended.

(2) The registrant previously paid a total of \$13,328.50 in connection with the previous filing of the registration statement. In accordance with Rule 457(a), no additional registration fee is being paid with this amendment to the registration statement.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

SUBJECT TO COMPLETION, DATED SEPTEMBER 25, 2017

PRELIMINARY PROSPECTUS

The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.



6,666,666 Shares

Rhythm Pharmaceuticals, Inc.

Common Stock

Rhythm Pharmaceuticals, Inc. is offering 6,666,666 shares of common stock. This is our initial public offering, and no public market currently exists for our common stock. We anticipate that the initial public offering price will be between \$14.00 and \$16.00 per share of common stock.

We have applied to have the common stock listed on the NASDAQ Global Market under the symbol "RYTM."

We are an "emerging growth company" under the federal securities laws and will be subject to reduced public company reporting requirements. Investing in our common stock involves risks. See "Risk Factors" beginning on page 16.

	<u>Per Share</u>	<u>Total</u>
Initial Public Offering Price	\$	\$
Underwriting Discount and Commissions ⁽¹⁾	\$	\$
Proceeds, before expenses, to us	\$	\$

(1) We refer you to "Underwriting" beginning on page 214 for additional information regarding underwriting compensation relating to reimbursement of certain legal fees and FINRA-related expenses.

Certain of our existing principal stockholders, directors and their affiliated entities, have indicated an interest in purchasing an aggregate of approximately \$40.0 million in shares of our common stock in this offering at the initial public offering price per share and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers, and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering. The underwriters will receive the same underwriting discount and commissions on these shares as they will on any other shares sold to the public in this offering.

We have granted the underwriters an option for a period of up to 30 days to purchase up to 1,000,000 additional shares of common stock.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares to purchasers on or about _____, 2017.

MORGAN STANLEY

BofA MERRILL LYNCH

COWEN

NEEDHAM & COMPANY

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We and the underwriters have not authorized anyone to provide any information or to make any representations other than those contained in this prospectus or in any free writing prospectuses we have prepared. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may provide you. We are offering to sell, and seeking offers to buy, shares of common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of the common stock.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our financial statements and the related notes included elsewhere in this prospectus. You should also consider, among other things, the matters described under "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," in each case appearing elsewhere in this prospectus. Unless otherwise stated, all references to "us," "our," "RYTM," "we," the "Company" and similar designations refer to Rhythm Pharmaceuticals, Inc. or our predecessor company, as the context may require. See "Corporate Reorganization."

Overview

We are a biopharmaceutical company focused on the development and commercialization of peptide therapeutics for the treatment of rare genetic deficiencies that result in life-threatening metabolic disorders. Our lead peptide product candidate is setmelanotide, a potent, first-in-class melanocortin-4 receptor, or MC4R, agonist for the treatment of rare genetic disorders of obesity. We believe setmelanotide, for which we have exclusive worldwide rights, has the potential to serve as replacement therapy for the treatment of melanocortin-4, or MC4, pathway deficiencies. MC4 pathway deficiencies result in the disruption of satiety signals and energy homeostasis in the body, which, in turn, leads to intense feelings of hunger and to obesity. Our development efforts are initially focused on obesity related to six single gene-related, or monogenic, MC4 pathway deficiencies—pro-opiomelanocortin, or POMC, leptin receptor, or LepR, Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous, and POMC epigenetic disorders—for which there are currently no effective or approved treatments. We believe that the MC4 pathway is a compelling target for treating these genetic disorders because of its critical role in regulating appetite and weight by promoting satiety and weight control, and that peptide therapeutics are uniquely suited for activating this target.

We have demonstrated proof of concept in Phase 2 clinical trials in POMC deficiency obesity, LepR deficiency obesity, and Bardet-Biedl syndrome, three genetic disorders of extreme and unrelenting appetite and obesity, in which setmelanotide dramatically reduced both weight and hunger. The U.S. Food and Drug Administration, or FDA, has acknowledged the importance of this preliminary clinical evidence by giving setmelanotide breakthrough therapy designation for the treatment of obesity associated with genetic defects upstream of the MC4 receptor in the leptin-melanocortin pathway, which includes both POMC deficiency obesity and LepR deficiency obesity. Setmelanotide is currently in Phase 3 development for POMC deficiency obesity and LepR deficiency obesity. We are currently enrolling patients in our POMC deficiency obesity Phase 3 clinical trial. We expect to complete enrollment by the end of 2017 and to report Phase 3 data in the first half of 2019. We expect to enroll the first patient in our LepR deficiency obesity Phase 3 clinical trial in the second half of 2017, and to complete enrollment in 2018. We recently demonstrated preliminary proof of concept in our Phase 2 clinical trial in Bardet-Biedl syndrome, indicating that this is also a setmelanotide-responsive, upstream MC4 pathway disorder. We are continuing to enroll patients in this trial and expect to report preliminary Phase 2 results in the fourth quarter of 2017. We expect to initiate a Phase 3 clinical trial in Bardet-Biedl syndrome in 2018. We have also initiated Phase 2 clinical trials in Alström syndrome, POMC heterozygous deficiency obesity and POMC epigenetic disorders, and expect to enroll patients in these trials in the second half of 2017. We anticipate reporting preliminary results in these additional Phase 2 indications in the first half of 2018.

Obesity is epidemic in the United States and current treatment approaches have demonstrated limited long-term success for most obese patients. We are taking a different approach to obesity drug development by leveraging new understanding of the genetic causes of severe obesity to develop innovative therapies that we believe have the potential for compelling efficacy. We believe we are at the forefront of improving treatment outcomes in subtypes of severe obesity that are caused by genetically-defined defects in the MC4 pathway.

Our Product Pipeline

The following chart depicts key information regarding the development of setmelanotide, including the indications we are pursuing within MC4 pathway deficiencies, the current state of development and our expected upcoming milestones:

Indication	PHASE 1	PHASE 2	PHASE 3	Proof-of-Concept	Last Event	Next Expected Event
POMC Deficiency Obesity			Green arrow pointing right	✓	Positive Phase 2; Phase 3 initiated	Phase 3 results 1H 2019
Leptin Receptor Deficiency Obesity			Green arrow pointing right	✓	Positive Phase 2; Phase 3 initiated	Phase 3 enrollment complete 2018
Bardet-Biedl Syndrome			Green arrow pointing right	✓	Preliminary proof of concept demonstrated	Preliminary Phase 2 results 4Q17; initiate Phase 3 2018
POMC Heterozygous Deficiency Obesity			Green arrow pointing right		Initiated Phase 2	Phase 2 results 1H 2018
Alström Syndrome			Green arrow pointing right		Initiated Phase 2	Phase 2 results 1H 2018
POMC Epigenetic Disorders			Green arrow pointing right		Initiated Phase 2	Phase 2 results 1H 2018

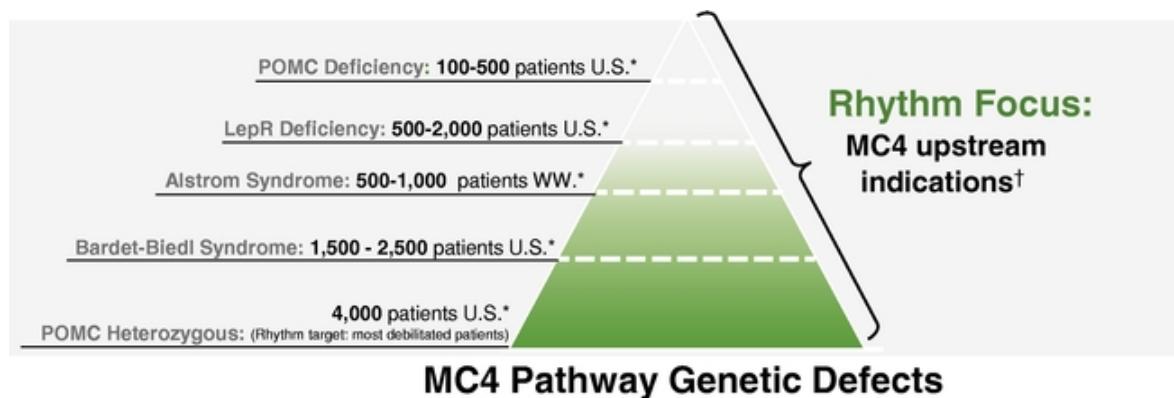
Setmelanotide: A First-in-Class MC4 Agonist

Setmelanotide is a potent, first-in-class, MC4R agonist peptide administered by daily subcutaneous, or SC, injection. Setmelanotide activates MC4R, which is part of the key pathway that can independently regulate energy homeostasis, which refers to the body's energy balance, and appetite. The critical role of the MC4 pathway in weight regulation was validated with the discovery that single genetic defects along this pathway result in early onset and severe obesity. An expanding set of severe obesity genetic defects are now identified that involve genes in the pathway which are either upstream of MC4R—for example POMC deficiency obesity and LepR deficiency obesity—or genes that are downstream of MC4R or affect MC4R itself. We are focusing setmelanotide clinical development on patients with monogenic upstream genetic defects in which obesity is life-threatening but the downstream MC4 pathway is fully functional. We believe setmelanotide has the potential to restore lost activity in the MC4 pathway by bypassing the defects upstream of MC4R, and activating the MC4 pathway below such defects. In this way, setmelanotide may serve as replacement therapy to reestablish weight and appetite control in patients with these genetic disorders.

The first generation MC4R agonists were small molecules that failed in clinical trials primarily due to safety issues, particularly increases in blood pressure, as well as limited efficacy. In contrast, setmelanotide is a peptide that retains the specificity and functionality of the naturally occurring hormone that activates MC4R. Approximately 275 obese subjects and patients have been treated with setmelanotide in previous and ongoing clinical trials in which setmelanotide demonstrated statistically significant weight loss with good tolerability.

Clinical Development in Rare Genetic Disorders of Obesity Caused by MC4 Pathway Deficiencies

The figure below summarizes the indications on which we are focusing for the development of setmelanotide, including our estimates for the addressable patient populations within these indications.



* The patient numbers above are based on company estimates.

† Epidemiological estimates are not yet available for POMC epigenetic disorders.

We believe that the patient populations in the European Union are at least as large as those in the United States. However, we do not have comparable epidemiological data from the European Union and these estimates are therefore based solely on applying relative population percentages to the Company-derived estimates described above.

POMC Deficiency Obesity

POMC deficiency obesity is a life-threatening, ultra-rare orphan disease, with approximately 50 patients reported to date. Ultra-rare orphan diseases are generally categorized as those that affect fewer than 20 patients per million. We estimate that our addressable patient population for this disorder is approximately 100 to 500 patients in the United States. Patients with POMC deficiency have unrelenting hunger, or hyperphagia, that begins in infancy and they develop severe, early onset obesity. POMC deficiency obesity is caused by the loss of both genetic copies of either the gene for POMC or the gene for proprotein convertase subtilisin/kexin 1, or PCSK, both upstream of MC4R, which results in loss of function in the MC4 pathway. Currently, there is no approved treatment for the obesity and hyperphagia associated with this genetic disorder.

We have initiated a Phase 3 open label, single arm, multinational trial to evaluate the safety and efficacy of setmelanotide for POMC deficiency obesity, with setmelanotide administered once daily by SC injection for 12 months. We are currently enrolling patients in this trial. We expect to complete enrollment by the end of 2017 and to report Phase 3 data in the first half of 2019. Previously, we completed a positive Phase 2 clinical trial in which two patients were enrolled and received treatment. The first patient in this trial lost 146.6 lbs over 118 weeks, from a baseline weight of 341.7 lbs, and the second patient lost 89.3 lbs over 64 weeks, from a baseline weight of 336.9 lbs. Both patients experienced substantial reductions in hunger, with hunger scores falling to one to two from baseline scores of nine to 10. Hunger scores were measured using a Likert score of zero to 10, where zero represents no hunger and 10 represents extreme hunger. Setmelanotide was generally well tolerated in this Phase 2 trial.

Leptin Receptor Deficiency Obesity

LepR deficiency obesity is an ultra-rare orphan disease that results in hyperphagia and severe early-onset obesity, with an estimated prevalence of 1% of subjects with severe, early-onset obesity. We estimate

that our addressable patient population for this disorder is approximately 500 to 2,000 patients in the United States. Like other deficiencies upstream in the MC4 pathway, LepR deficiency results in loss of function in the MC4 pathway. Therefore, patients with this indication also manifest hyperphagia and severe obesity from early childhood. Currently, there is no approved treatment for the obesity and hyperphagia associated with this genetic disorder.

We have initiated a Phase 3 open label, single arm, multinational trial to evaluate the safety and efficacy of setmelanotide for LepR deficiency obesity, with setmelanotide administered once daily by SC injection for 12 months. We expect to enroll the first patient in our LepR deficiency obesity Phase 3 clinical trial in the second half of 2017, and to complete enrollment in 2018. Previously, we completed a positive Phase 2 clinical trial in which three patients were enrolled and received treatment in this trial each experiencing significant weight loss and substantial reductions in hunger. Setmelanotide was generally well tolerated in this Phase 2 trial.

Bardet-Biedl syndrome

Bardet-Biedl syndrome is a life-threatening, ultra-rare orphan disease with a prevalence of approximately one in 100,000 in North America. We estimate that our addressable patient population for Bardet-Biedl syndrome obesity is approximately 1,500 to 2,500 patients in the United States. Bardet-Biedl syndrome is a monogenic disorder that causes severe obesity and hyperphagia as well as vision loss, polydactyly, kidney abnormalities, and other signs and symptoms. Currently there are no approved or effective therapies for Bardet-Biedl syndrome.

We recently demonstrated preliminary proof of concept in our Phase 2 clinical trial in Bardet-Biedl syndrome, indicating that this is also a setmelanotide-responsive, upstream MC4 pathway disorder. We are continuing to enroll patients in this trial and expect to report preliminary Phase 2 results in the fourth quarter of 2017. We expect to initiate a Phase 3 clinical trial in Bardet-Biedl syndrome in 2018.

Other Upstream Genetic Defects in the MC4 Pathway

We are also focusing on additional monogenic, upstream MC4 pathway deficiencies for which setmelanotide can function as replacement therapy and provide activation of the pathway downstream of the defect, promoting satiety and weight control. We have initiated Phase 2 trials for Alström syndrome, a life-threatening, ultra-rare orphan disease, for which we estimate our addressable population is approximately 500 to 1,000 patients worldwide, for POMC heterozygous deficiency obesity, for which we estimate our addressable population is approximately 4,000 patients in the United States, and for POMC epigenetic disorders. For these patients, hyperphagia and obesity can have significant health consequences for which there is currently no approved treatment. We expect to enroll patients with Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders in the second half of 2017 and to report preliminary results from these trials in the first half of 2018.

Expanding Attention to the Diagnosis of Genetic Obesity

We are supporting several initiatives to expand the diagnosis of genetic obesity, including The Genetic Obesity Project. The Genetic Obesity Project has initiated a genotyping study, or GO-ID genotyping study, and a patient registry, or GO-ID registry, both focusing initially on identifying people with POMC deficiency obesity and LepR deficiency obesity, and we are currently including other MC4 pathway deficiencies. Our preliminary results in 560 genotyped patients suggest we can successfully identify these patients. We have also conducted a genetic obesity epidemiology analysis of MC4 pathway genetic defects in a large representative sample of the U.S. population. Based on preliminary findings from this analysis, we believe the prevalence of these MC4 pathway deficiencies within the U.S. population could be substantially larger than our current estimates. We plan to continue our work in analyzing and assessing the epidemiology for these rare genetic disorders of obesity.

Breakthrough Therapy and Orphan Designations

Based on our POMC deficiency obesity and LepR deficiency obesity Phase 2 results, the FDA granted setmelanotide breakthrough therapy designation for the treatment of obesity associated with genetic defects upstream of the MC4 receptor in the leptin-melanocortin pathway, which includes both POMC deficiency obesity and LepR deficiency obesity, enabling an expedited path to approval of setmelanotide for these two indications. In April 2016, the FDA granted our orphan drug designation request for setmelanotide for the treatment of POMC deficiency obesity.

Company History

Our company was founded in November 2008 by former biopharmaceutical executives who have successfully developed, commercialized and in-licensed innovative pharmaceutical products, and we have subsequently expanded our senior management team to further broaden our team's experience in developing, registering and commercializing new drugs. In addition, our scientific advisory board, or SAB, members have extensive clinical expertise in obesity, endocrinology and metabolic diseases. We intend to leverage the experience of our senior management team and SAB to develop and commercialize setmelanotide. Through our senior management team's network of industry contacts, we will continue to evaluate additional product candidate licensing and acquisition opportunities. We are backed by strong and dedicated investors that include both private equity venture capital funds and public healthcare investment funds. Our investors include MPM Capital, New Enterprise Associates, Third Rock Ventures, Ipsen, Pfizer Venture Investments, OrbiMed, Deerfield Management and two public healthcare investment funds.

Our patent portfolio includes composition of matter patents for setmelanotide that expire in the United States in 2027, with possible patent term extension to 2032 under the Hatch-Waxman Act.

Our Strategy

Our goal is to be a leader in developing and commercializing targeted therapies for genetic deficiencies that result in life-threatening metabolic disorders. The key components of our strategy are:

- **Rapidly develop setmelanotide for rare genetic disorders of obesity caused by MC4 pathway deficiencies.** We are aiming to dramatically improve patient outcomes in severe obesity by targeting setmelanotide's mechanism of action to the treatment of patients with genetically-defined defects in the MC4 pathway. We are focusing setmelanotide clinical development on monogenic upstream genetic defects in which obesity is life-threatening but where the downstream MC4 pathway is fully functional.
- **Advance setmelanotide for POMC deficiency obesity and LepR deficiency obesity as our first indications in upstream MC4 pathway deficiencies.** We currently have a Phase 3 trial underway for POMC deficiency obesity and expect to report Phase 3 data in the first half of 2019. We have also initiated a Phase 3 trial for LepR deficiency obesity. We expect to enroll the first patient in our LepR deficiency obesity Phase 3 clinical trial in the second half of 2017, and to complete enrollment in 2018.
- **Expand setmelanotide development to additional upstream MC4 pathway deficiencies, including Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders.** We have initiated Phase 2 clinical trials in these rare genetic disorders, and have obtained preliminary proof of concept in Bardet-Biedl syndrome demonstrating that this is also a setmelanotide-responsive, upstream MC4 pathway disorder. We anticipate reporting these preliminary results for Bardet-Biedl syndrome in the fourth quarter of 2017, starting Phase 3 clinical trials in 2018, and obtaining preliminary results for the other Phase 2 indications in the first half of 2018.

- **Commercialize setmelanotide for rare disease indications in core strategic markets.** We intend to establish our own commercial sales and marketing organization in the United States and other core strategic markets. We may also selectively establish partnerships in markets outside the United States for sales, marketing and distribution.
- **Leverage the broad experience of our team in clinical and commercial drug development, and product acquisitions.** We will apply our team's extensive experience in developing and commercializing innovative medicines to the development and launch of setmelanotide. In addition, we intend to identify and acquire new pipeline programs in related diseases.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the "Risk Factors" section beginning on page 16 of this prospectus. These risks include the following:

- We are a development stage biopharmaceutical company with a limited operating history and have not generated any revenue from product sales. We have incurred significant operating losses since our inception, anticipate that we will incur continued losses for the foreseeable future and may never achieve profitability. As of June 30, 2017, we had an accumulated deficit of \$89.7 million.
- Even if this offering is successful, we will need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.
- We have only one product candidate and we may not be successful in any future efforts to identify and develop additional product candidates.
- Positive results from early clinical trials of setmelanotide may not be predictive of the results of later clinical trials of setmelanotide. If we cannot generate positive results in our later clinical trials of setmelanotide, we may be unable to successfully develop, obtain regulatory approval for and commercialize setmelanotide.
- The number of patients suffering from each of the MC4 pathway deficiencies is small and has not been established with precision. If the actual number of patients with any of these conditions is smaller than we had estimated, our revenue and ability to achieve profitability will be materially adversely affected.
- Failures or delays in the commencement or completion of our planned clinical trials of setmelanotide could result in increased costs to us and could delay, prevent or limit our ability to generate revenue and continue our business.
- Changes in regulatory requirements, FDA guidance or unanticipated events during our clinical trials of setmelanotide may occur, which may result in changes to clinical trial protocols or additional clinical trial requirements, which could result in increased costs to us and could delay our development timeline. Additionally, it may be necessary to validate different or additional instruments for measuring subjective symptoms, and to show that setmelanotide has a clinically meaningful impact on those endpoints in order to obtain regulatory approval.
- Even if we complete the necessary clinical trials, the regulatory and marketing approval process is expensive, time consuming and uncertain and may prevent us from obtaining approvals for the commercialization of setmelanotide. We depend almost entirely on the success of setmelanotide, which is still in clinical development. We cannot be certain that we will be able to obtain regulatory approval for, or successfully commercialize setmelanotide. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize setmelanotide and our ability to generate revenue will be materially impaired.

- If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.
- Setmelanotide may cause undesirable side effects that could delay or prevent its regulatory approval, limit the commercial profile of an approved labeling or result in significant negative consequences following marketing approval, if any.
- Even if approved, reimbursement policies could limit our ability to sell setmelanotide.
- Competing products and technologies could emerge, adversely affecting our opportunity to generate revenue from the sale of setmelanotide.
- If we are unable to obtain and maintain patent protection for setmelanotide and its related technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and setmelanotide may be impaired.
- Since we have only a limited history of operating as an independent company, we may incur unforeseen expenses associated with doing so.

Corporate Reorganization and Other Information

We are a Delaware corporation organized in February 2013 under the name Rhythm Metabolic, Inc. and as of October 2015, under the name Rhythm Pharmaceuticals, Inc. Prior to our organization and the Corporate Reorganization referred to below, we were part of Rhythm Pharmaceuticals, Inc., a Delaware corporation which was organized in November 2008 and which commenced active operations in 2010. We refer to this corporation as the Predecessor Company.

In March 2013, the Predecessor Company underwent a corporate reorganization, which we refer to as the Corporate Reorganization, pursuant to which all of the outstanding equity securities of the Predecessor Company were exchanged for units of Rhythm Holding Company, LLC, a newly-organized limited liability company, which we refer to as the LLC entity. After the consummation of this exchange and as part of the Corporate Reorganization, the Predecessor Company contributed setmelanotide and the MC4R agonist program to us and distributed to the LLC entity all of the then issued and outstanding shares of our stock. The result of the Corporate Reorganization was that we and the Predecessor Company became wholly-owned subsidiaries of the LLC entity and the two product candidates and related programs that were originally held by the Predecessor Company were separated, with relamorelin and the ghrelin agonist program being retained by the Predecessor Company and setmelanotide and the MC4R agonist program being held by us. We refer to the Predecessor Company after consummation of the Corporate Reorganization as the Relamorelin Company. The Predecessor Company filed the IND for setmelanotide in October 2011 and conducted the setmelanotide clinical trials up until the Corporate Reorganization, after which all clinical trials have been conducted by us.

In October 2014, the LLC entity granted to Actavis plc, now owned by Allergan, Inc., or Allergan, an exclusive option to acquire the Relamorelin Company. The transaction was limited to the acquisition of the Relamorelin Company and did not include our company. In October 2016, the option to acquire the Relamorelin Company was exercised and the sale to Allergan closed on December 15, 2016.

In August 2015, we effected a 93,500-for-1 forward stock split of our then-outstanding common stock. Also in August 2015, December 2015, January 2017 and August 2017, we sold 25,000,000 shares, 15,000,000 shares, 20,475,001 shares and 20,474,998 shares, respectively, of our series A preferred stock to certain investors. Following the stock split and the closing of our series A preferred stock financings, the LLC entity remained our largest stockholder, with the balance of our stock being owned by our series A investors. In August 2017, the LLC entity exchanged 8,578,646 of its shares of our common stock for 78,666,209 newly-issued shares of our series A-1 junior preferred stock and the LLC entity distributed all

of its shares of our series A-1 junior preferred stock to the holders of its preferred units and the remaining 1,617,646 shares of our common stock to the holders of its common units. We refer to the exchange and distribution as the Distribution. The series A-1 junior preferred stock will convert into shares of our common stock on a 9.17-for-1 basis upon the closing of this offering. Following the Distribution, the LLC entity no longer owns any of our common stock.

In connection with the offering, we will effect a 1-for-9.17 reverse stock split of our outstanding common stock.

On October 13, 2015, the Relamorelin Company changed its name to Motus Therapeutics, Inc. and we changed our name to Rhythm Pharmaceuticals, Inc.

Our principal executive offices are located at 500 Boylston Street, 11th Floor, Boston, MA 02116, and our telephone number is (857) 264-4280. Our corporate website address is www.rhythmtx.com. Information contained on or accessible through our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is an inactive textual reference only.

This prospectus contains references to our trademarks and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to in this prospectus, including logos, artwork and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

Implications of Being an Emerging Growth Company

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of this offering, (b) in which we have total annual gross revenue of at least \$1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior June 30th, and (2) the date on which we have issued more than \$1.0 billion in non-convertible debt securities during the prior three-year period. We refer to the Jumpstart Our Business Startups Act of 2012 in this prospectus as the "JOBS Act," and references in this prospectus to "emerging growth company" shall have the meaning ascribed to it in the JOBS Act.

An emerging growth company may take advantage of reduced reporting requirements that are otherwise applicable to public companies. These provisions include, but are not limited to:

- the ability to present only two years of audited financial statements and only two years of related Management's Discussion and Analysis of Financial Condition and Results of Operations in this prospectus;
- an exemption from the requirements to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended;
- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements; and
- exemptions from the requirement to hold a nonbinding advisory vote on executive compensation and to obtain stockholder approval of any golden parachute payments not previously approved.

We may use these provisions until such time as we cease to be an emerging growth company.

We have elected to take advantage of certain of the reduced disclosure obligations in the registration statement of which this prospectus forms a part and may elect to take advantage of other reduced reporting requirements in future filings. As a result, the information that we provide to our stockholders may be different from the information that you might receive from other public reporting companies in which you hold equity interests.

The JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. We have irrevocably elected not to avail ourselves of this exemption and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

THE OFFERING

Common stock offered by us	6,666,666 shares
Common stock to be outstanding after this offering	25,690,650 shares
Option to purchase additional common stock offered by us	1,000,000 shares
Use of proceeds	We estimate that our net proceeds from this offering will be approximately \$90.6 million at an assumed initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds from this offering, together with our existing cash resources, as follows: <ul style="list-style-type: none">• approximately \$17 million to fund the development and manufacturing of setmelanotide through completion of our Phase 3 clinical trials and subsequent NDA submissions with the FDA for the treatment of POMC deficiency obesity and LepR deficiency obesity;• approximately \$14 million for the development of setmelanotide through completion of our Phase 2 proof of concept clinical trials for Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity and POMC epigenetic disorders, as well as the initiation of our Phase 3 clinical trial for Bardet-Biedl syndrome;• approximately \$16 million for initiatives to expand the diagnosis of genetic obesity, including research and scientific exchange related to our ongoing genotyping and genetic epidemiology studies;• approximately \$38 million for preparation for commercialization of setmelanotide; and• the remainder for general working capital and administrative expenses, additional research and development expenses, and other general corporate purposes.
Risk factors	See "Risk Factors" beginning on page 16 and the other information included in this prospectus for a discussion of factors you should carefully consider before deciding to invest in our common stock.
Proposed NASDAQ Global Market Symbol	"RYTM"

The number of shares of our common stock to be outstanding after this offering is based on 19,023,984 shares of our common stock outstanding as of June 30, 2017 and assumes:

- a 1-for-9.17 reverse stock split of our common stock, to be effective immediately prior to the effectiveness of the registration statement of which this prospectus forms a part;

- the conversion of all our outstanding preferred stock into 17,406,338 shares of our common stock upon the completion of this offering;
- no exercise by the underwriters of their option to purchase additional shares of common stock; and
- the filing of our amended and restated certificate of incorporation upon the closing of this offering.

In this prospectus, unless otherwise indicated, the number of shares of common stock outstanding as of June 30, 2017 and the other information based thereon does not reflect:

- 152,671 shares of common stock issued upon the exercise of stock options after June 30, 2017;
- 2,196,958 shares of common stock that will be reserved for future issuance under our 2017 equity incentive plan, or the 2017 Plan;
- 258,433 shares of common stock that will be reserved for future issuance under our 2017 employee stock purchase plan; and
- 1,821,580 shares of common stock issuable upon the exercise of stock options outstanding as of September 25, 2017 under our 2015 equity incentive plan, as amended and in effect until the closing of this offering, or the 2015 Plan, at a weighted average exercise price of \$5.99.

Indications of Interest

Certain of our existing principal stockholders, directors and their affiliated entities, have indicated an interest in purchasing an aggregate of approximately \$40.0 million in shares of our common stock in this offering at the initial public offering price per share and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers, and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering. The underwriters will receive the same underwriting discount and commissions on these shares as they will on any other shares sold to the public in this offering.

SUMMARY FINANCIAL DATA

The following summary financial data for the years ended December 31, 2015 and 2016 are derived from our audited financial statements included elsewhere in this prospectus. The summary financial data as of June 30, 2017 and for the six months ended June 30, 2016 and 2017 have been derived from our unaudited financial statements included elsewhere in this prospectus. These unaudited financial statements have been prepared on a basis consistent with our audited financial statements and, in our opinion, contain all adjustments, consisting only of normal and recurring adjustments, necessary for a fair presentation of such financial data. You should read this data together with our audited financial statements and related notes included elsewhere in this prospectus and the information under the captions "Selected Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations." Our historical results are not necessarily indicative of our future results, and our operating results for the six-month period ended June 30, 2017 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2017 or any other interim periods or any future year or period.

Our financial statements for the periods presented include allocations of costs from certain shared functions provided to us by the Relamorelin Company. These allocations were made based on either a specific identification basis or, when a specific identification is not practicable, a proportional cost allocation method which allocates expenses based on the percentage of employee time and research and development efforts expended on our business as compared to total employee time and research and development efforts, and have been included in our financial statements for the periods presented.

The financial statements included in this prospectus may not necessarily reflect our financial position, results of operations and cash flows as if we had operated as an independent company during all of the periods presented. See "Corporate Reorganization."

	Year Ended December 31,		Six Months Ended June 30,	
	2015	2016	2016	2017
	(in thousands, except share and per share data)			
Operating expenses:				
Research and development	\$ 7,148	\$ 19,594	\$ 8,544	\$ 10,270
General and administrative	3,425	6,311	2,585	2,873
Total operating expenses	<u>10,573</u>	<u>25,905</u>	<u>11,129</u>	<u>13,143</u>
Loss from operations	(10,573)	(25,905)	(11,129)	(13,143)
Other income (expense):				
Revaluation of Series A Investor Right/Obligation and Series A Investor Instrument	(500)	—	—	(82)
Interest income, net	—	33	14	63
Total other income (expense):	<u>(500)</u>	<u>33</u>	<u>14</u>	<u>(19)</u>
Net loss and comprehensive loss	\$ (11,073)	\$ (25,872)	\$ (11,115)	\$ (13,162)
Net loss attributable to common stockholders	<u>\$ (12,000)</u>	<u>\$ (29,074)</u>	<u>\$ (12,711)</u>	<u>\$ (15,534)</u>
Net loss attributable to common stockholders per common share, basic and diluted ⁽¹⁾	\$ (1.18)	\$ (2.85)	\$ (1.25)	\$ (1.52)
Weighted average common shares outstanding, basic and diluted	<u>10,196,292</u>	<u>10,196,292</u>	<u>10,196,292</u>	<u>10,196,292</u>
Pro forma net loss attributable to common stockholders per common share, basic and diluted (unaudited) ⁽¹⁾	\$ (1.78)		\$ (0.79)	
Pro forma weighted average common shares outstanding, basic and diluted (unaudited) ⁽¹⁾	<u>14,558,342</u>		<u>16,729,487</u>	

	As of June 30, 2017			Pro Forma As Adjusted ⁽³⁾ (unaudited in thousands)
	Actual	Pro Forma ⁽²⁾		
Balance Sheet Data:				
Cash, cash equivalents and short-term investments	\$ 17,740	\$ 38,215	\$ 128,815	
Working capital	13,619	34,094	124,694	
Total assets	20,404	40,879	131,479	
Convertible preferred stock	60,147	—	—	
Accumulated deficit	(89,705)	(89,705)	(89,705)	
Total stockholders' equity (deficit)	\$ (45,266)	\$ 35,766	\$ 126,366	

- (1) See Note 2 within the notes to our financial statements appearing elsewhere in this prospectus for a description of the methods used to calculate basic and diluted net loss per share and pro forma basic and diluted net loss per share.
- (2) Pro forma to reflect the issuance of 78,666,209 shares of our series A-1 junior preferred stock in exchange for 8,578,646 shares of our common stock in connection with the Distribution, the issuance

of 20,474,998 shares of series A preferred stock in August 2017 (see Note 12 within the notes to our financial statements appearing elsewhere in this prospectus) and the conversion of all of our outstanding preferred stock into 17,406,338 shares of common stock upon the closing of this offering.

- (3) Pro forma as adjusted to further reflect the issuance and sale of 6,666,666 shares of our common stock in this offering, at an assumed initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

CORPORATE REORGANIZATION

We are a Delaware corporation organized in February 2013 under the name Rhythm Metabolic, Inc. and as of October 2015, under the name Rhythm Pharmaceuticals, Inc. Prior to our organization and the Corporate Reorganization referred to below, we were part of Rhythm Pharmaceuticals, Inc., a Delaware corporation which was organized in November 2008 and which commenced active operations in 2010. We refer to this corporation as the Predecessor Company.

In March 2013, the Predecessor Company underwent a corporate reorganization, which we refer to as the Corporate Reorganization, pursuant to which all of the outstanding equity securities of the Predecessor Company were exchanged for units of Rhythm Holding Company, LLC, a newly-organized limited liability company, which we refer to as the LLC entity. After the consummation of this exchange and as part of the Corporate Reorganization, the Predecessor Company contributed setmelanotide and the MC4R agonist program to us and distributed to the LLC entity all of the then issued and outstanding shares of our stock. The result of the Corporate Reorganization was that we and the Predecessor Company became wholly-owned subsidiaries of the LLC entity and the two product candidates and related programs that were originally held by the Predecessor Company were separated, with relamorelin and the ghrelin agonist program being retained by the Predecessor Company and setmelanotide and the MC4R agonist program being held by us. We refer to the Predecessor Company after consummation of the Corporate Reorganization as the Relamorelin Company. The Predecessor Company filed the IND for setmelanotide in October 2011 and conducted the setmelanotide clinical trials up until the Corporate Reorganization, after which all clinical trials have been conducted by us.

In October 2014, the LLC entity granted to Actavis plc, now owned by Allergan, Inc., or Allergan, an exclusive option to acquire the Relamorelin Company. The transaction was limited to the acquisition of the Relamorelin Company and did not include us. In October 2016, the option to acquire the Relamorelin Company was exercised and the sale to Allergan closed on December 15, 2016.

In August 2015, we effected a 93,500-for-1 forward stock split of our then-outstanding common stock. Also in August 2015, December 2015, January 2017 and August 2017, we sold 25,000,000 shares, 15,000,000 shares, 20,475,001 shares and 20,474,998 shares, respectively, of our series A preferred stock to certain investors. Following the stock split and the closing of our series A preferred stock financings, the LLC entity remained our largest stockholder, with the balance of our stock being owned by our series A investors. In August 2017, the LLC entity exchanged 8,578,646 of its shares of our common stock for 78,666,209 newly-issued shares of our series A-1 junior preferred stock and the LLC entity distributed all of its shares of our series A-1 junior preferred stock to the holders of its preferred units and the remaining 1,617,646 shares of our common stock to the holders of its common units. We refer to the exchange and distribution as the Distribution. The series A-1 junior preferred stock will convert into shares of our common stock on a 9.17-for-1 basis upon the closing of this offering. Following the Distribution, the LLC entity no longer owns any of our common stock.

On September 22, 2017, the Board of Directors approved a 1-for-9.17 reverse stock split of the Company's common stock. All share and per share information included in the accompanying financial statements has been adjusted to reflect this reverse stock split.

Prior to the sale of the Relamorelin Company to Allergan, we had an Amended and Restated Payroll Services Agreement with the Relamorelin Company, which we refer to as the Payroll Services Agreement. Pursuant to the Payroll Services Agreement, the Relamorelin Company provided us certain employee and consultant services. We had five employees whose services were provided to us pursuant to this agreement. We also shared certain costs with the Relamorelin Company, including finance, accounting, research and development and operations. As part of the sale of the Relamorelin Company, these employees became our employees and have employment agreements with us.

On October 13, 2015, the Relamorelin Company changed its name to Motus Therapeutics, Inc. and we changed our name to Rhythm Pharmaceuticals, Inc.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the following risks and uncertainties, together with all other information in this prospectus, including our financial statements and related notes, before investing in our common stock. Any of the risk factors we describe below could adversely affect our business, financial condition or results of operations. The market price of our common stock could decline if one or more of these risks or uncertainties actually occur, causing you to lose all or part of the money you paid to buy our common stock. Additional risks that we currently do not know about or that we currently believe to be immaterial may also impair our business. Certain statements below are forward-looking statements. See "Cautionary Note Regarding Forward-Looking Statements" in this prospectus.

Risks Related to Our Financial Position and Need for Capital

We are a clinical-stage biopharmaceutical company with a limited operating history and have not generated any revenue from product sales. We have incurred significant operating losses since our inception, anticipate that we will incur continued losses for the foreseeable future and may never achieve profitability.

We are a clinical-stage biopharmaceutical company with a limited operating history on which to base your investment decision. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We were incorporated in February 2013 in connection with the Corporate Reorganization. Our operations to date have been limited primarily to acquiring rights to intellectual property, business planning, raising capital, developing our technology, identifying potential product candidates, undertaking preclinical studies and conducting research and development activities, including clinical trials, for setmelanotide. We have never generated any revenue from product sales. We have not obtained any regulatory approvals for setmelanotide.

Since our inception, we have focused substantially all of our efforts and financial resources on the research and development of setmelanotide, which is currently in Phase 3 clinical development for two indications, POMC deficiency obesity and LepR deficiency obesity, and in various phases of development for other indications. We have funded our operations to date primarily through capital contributions from the Predecessor Company, the Relamorelin Company and the LLC entity and proceeds from sales of preferred stock and have incurred losses in each year since our inception.

Our net loss and comprehensive losses were \$11.1 million, \$25.9 million, \$11.1 million and \$13.2 million for the years ended December 31, 2015 and 2016 and the six months ended June 30, 2016 and 2017, respectively. As of June 30, 2017, we had an accumulated deficit of \$89.7 million. Substantially all of our operating losses have resulted from costs incurred in connection with our development program and from general and administrative costs associated with our operations. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' deficit and working capital. We expect our research and development expenses to significantly increase in connection with our additional clinical trials of setmelanotide and development of any other product candidates we may choose to pursue. In addition, if we obtain marketing approval for setmelanotide, we will incur significant sales, marketing and outsourced manufacturing expenses. Once we are a public company, we will incur additional costs associated with operating as a public company. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue from setmelanotide, and we do not know when, or if, we will generate any revenue. We do not expect to generate significant revenue unless and until we obtain marketing approval for, and

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begin to sell, setmelanotide. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to:

- initiate and successfully complete later-stage clinical trials that meet their clinical endpoints;
- initiate and successfully complete all safety studies required to obtain U.S. and foreign marketing approval for setmelanotide as a treatment for obesity caused by genetic deficiencies affecting the MC4 pathway;
- successfully manufacture or contract with others to manufacture setmelanotide;
- commercialize setmelanotide, if approved, by building an internal sales force or entering into collaborations with third parties; and
- achieve market acceptance of setmelanotide in the medical community and with third-party payors.

Absent our entering into collaboration or partnership agreements, we expect to incur significant sales and marketing costs as we prepare to commercialize setmelanotide. Even if we initiate and successfully complete our pivotal clinical trials and setmelanotide is approved for commercial sale, and we incur the costs associated with these activities, setmelanotide may not be a commercially successful drug. We may not achieve profitability soon after generating product sales, if ever. If we are unable to generate product revenue, we will not become profitable and will be unable to continue operations without continued funding.

Even if this offering is successful, we will need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

We are currently advancing setmelanotide through clinical development. Developing peptide therapeutic products is expensive, and we expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we advance setmelanotide in clinical trials. We intend to use the proceeds of this offering primarily for the clinical development and regulatory approval of setmelanotide. Depending on the status of regulatory approval and, if approved, commercialization of setmelanotide, as well as the progress we make in the sale of setmelanotide, we may still require significant additional capital to fund the continued development of setmelanotide and our operating needs thereafter. We may also need to raise additional funds if we choose to pursue additional indications and/or geographies for setmelanotide or otherwise expand more rapidly than we presently anticipate.

Through August 2015, we received capital contributions from the Predecessor Company, the Relamorelin Company and the LLC entity. In August 2015, December 2015, January 2017 and August 2017, we raised aggregate gross proceeds of \$25.0 million, \$15.0 million, \$20.5 million and \$20.5 million, respectively, through our issuance of series A preferred stock. As of June 30, 2017, our cash and cash equivalents and short-term investments were approximately \$17.7 million and after giving effect, on a pro forma basis, to the aggregate gross proceeds from the sale of our series A preferred stock in August 2017, \$38.2 million. We estimate that the net proceeds from this offering will be approximately \$90.6 million, assuming an initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and offering expenses payable by us. We expect that the net proceeds from this offering, together with our existing cash and cash equivalents, will be sufficient to fund our operating expenses into the first half of 2019. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements, or a combination of these approaches. We will also require additional capital to obtain regulatory approval for, and to commercialize, setmelanotide. Raising funds in the current economic environment may present additional challenges. Even if we believe

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we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize setmelanotide. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights, and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborative partners or other third parties at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to setmelanotide or technologies or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of setmelanotide or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially adversely affect our business, financial condition and results of operations.

Our auditors have issued a "going concern" audit opinion.

Our independent auditors have indicated in their report on our December 31, 2016 financial statements, that there is substantial doubt about our ability to continue as a going concern. A "going concern" opinion indicates that the financial statements have been prepared assuming we will continue as a going concern and do not include any adjustments to reflect the possible future effects on the recoverability and the classification of assets, or the amounts and classification of liabilities that may result if we do not continue as a going concern. Therefore, you should not rely on our balance sheet as an indication of the amount of proceeds that would be available to satisfy claims of creditors, and potentially be available for distribution to shareholders, in the event of a liquidation. The inclusion of a going concern explanatory paragraph by our auditors, our lack of cash resources and our potential inability to continue as a going concern may materially adversely affect our share price and our ability to raise new capital or to enter into critical contractual relationships with third parties.

Our very limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We are an early-stage company. The Predecessor Company commenced active operations in February 2010, and we were incorporated as a separate company in February 2013. Our operations to date have been limited primarily to acquiring rights to intellectual property, business planning, raising capital, developing our technology, identifying potential product candidates, undertaking preclinical studies and, beginning in November 2010, conducting clinical trials. We have not yet demonstrated our ability to successfully complete a pivotal Phase 3 clinical trial, obtain marketing approvals, manufacture at commercial scale, or arrange for a third party to do so on our behalf or conduct sales, marketing and distribution activities necessary for successful product commercialization. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition at some point from a company

with a research and development focus to a company capable of supporting commercial activities and we may not be successful in such a transition.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter-to-quarter and year-to-year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

Our historical and pro forma financial information is not necessarily representative of the results we would have achieved as an independent company, and may not be a reliable indicator of our future results.

The historical financial and pro forma financial information we have included in this prospectus may not reflect what our results of operations, financial position and cash flows would have been had we been an independent company during the periods presented. This is primarily because:

- our historical financial information reflects allocations for services historically provided to us by the Predecessor Company and the Relamorelin Company, which allocations may not reflect the costs we now and in the future will incur for similar services as an independent company; and
- our historical financial information does not reflect changes that we have incurred and expect to continue to incur as a result of operating as an independent company and from reduced economies of scale, including changes in cost structure, personnel needs, financing and operations of our business.

In addition, the pro forma financial information included in this prospectus is based on the best information available, which in part includes a number of estimates and assumptions which may prove to be inaccurate. Accordingly, our pro forma financial information should not be assumed to be indicative of what our financial condition or results of operations actually would have been as an independent company, nor to be a reliable indicator of what our financial condition or results of operations may actually be in the future. See "Management's Discussion and Analysis of Financial Condition and Results of Operations."

Risks Related to the Development of Setmelanotide

Positive results from early clinical trials of setmelanotide may not be predictive of the results of later clinical trials of setmelanotide. If we cannot generate positive results in our later clinical trials of setmelanotide, we may be unable to successfully develop, obtain regulatory approval for, and commercialize setmelanotide.

Positive results from any of our Phase 1 and Phase 2 clinical trials of setmelanotide may not be predictive of the results of later clinical trials. The duration of effect of setmelanotide tested in our Phase 1 and Phase 2 clinical trials was often for shorter periods than that planned for testing in our current pivotal Phase 3 clinical trials. The duration of effect of setmelanotide has only been studied in long-term durations for a small number of patients in our Phase 2 clinical trials and safety or efficacy issues may arise when more patients are studied in longer trials. It is possible that the effects seen in short-term clinical trials will not be replicated in long-term or larger clinical trials. In addition, not all of our trials demonstrated statistically significant weight loss and there can be no guarantee that future trials will do so.

Positive results for one indication are not necessarily predictive of positive results for other indications. We have demonstrated proof of concept in Phase 2 clinical trials in POMC deficiency obesity, LepR deficiency obesity, and Bardet-Biedl syndrome, three genetic disorders of extreme and unrelenting appetite and obesity, in which setmelanotide dramatically reduced both weight and hunger. We hypothesize that patients with other upstream genetic defects in the MC4 pathway may also respond with reductions in weight and hunger after treatment with setmelanotide, however patients with other upstream genetic defects may not have a similar response to setmelanotide, and until we obtain more clinical data in other genetic defects, we will not be sure that we can achieve proof of concept in such indications. In addition, while we believe that proof of concept in Bardet-Biedl syndrome has been demonstrated by improvements in hunger and weight reduction, supporting that this is a setmelanotide-responsive, MC4 pathway disorder, the results of this trial are still at a preliminary stage.

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We have or will have multiple clinical trials of setmelanotide ongoing, which are designed to include multiple genetically and clinically defined populations under one investigational protocol, although each population is enrolled and analyzed separately. A "basket" trial design could potentially decrease the time to study new populations by decreasing administrative burden, however, these trials do not overcome limitations to extrapolating data from the experience in one disease to other diseases, because safety and efficacy results in each indication are analyzed separately. Accordingly, clinical success in a basket trial, or any trial in one indication, may not predict success in another indication. In the event of an adverse safety issue, clinical hold or other adverse finding in one or more indications being tested, such event could adversely affect our trials in the other indications and may delay or prevent completion of the clinical trials.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials after achieving positive results in early stage development, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, pre—clinical findings made while clinical trials were underway. We have completed the key toxicology studies that we believe the U.S. Food and Drug Administration, or the FDA, and the European Medicines Agency, or EMA, will require for approval, which include, among others, chronic toxicity studies, reproductive and developmental toxicity studies, and juvenile toxicology studies. Based on the totality of animal testing results to date, including the lack of any observed genotoxicity or tissue proliferative activity of setmelanotide in chronic toxicity studies, we have requested that the FDA permit us to defer carcinogenicity studies until after approval of a new drug application, or NDA, for setmelanotide. Accordingly, we believe that we will be able to defer all carcinogenicity studies until after we receive regulatory approval to market setmelanotide. However, the FDA has indicated that it will not make a decision on our request until after reviewing our final toxicology study reports. Accordingly, at this time, there can be no guarantee that we will be able to achieve this deferral which could impact the timing of any potential NDA approval as well as the time frame to achieve commercialization.

In addition to the foregoing issue, the FDA has requested that in our chronic rat and monkey studies we assess certain cells in brain, renal and liver tissues for the presence of vacuoles, which are common membrane-bound compartments. The recommendation was based on the FDA's review of a summary of a rat study that noted the presence of macrophage aggregates, which are groupings of specific white blood cells, in the choroid plexus, a network of blood vessels and epithelial tissue in the membrane lining outside the brain and spinal cord. The FDA noted that the existence of macrophage aggregates appears to be related to the polyethylene glycol vehicle in the product, rather than setmelanotide itself. We do not believe that the appearance of these aggregates raises any safety concerns, in part because of the localization of these aggregates. However, the FDA has indicated that they agree with our position, and, accordingly, we are performing additional assessments for the presence of vacuoles, including assessments by an independent pathologist. Despite these additional assessments, the FDA may still not agree with our interpretation, and may require us to reflect these findings in the toxicological portion of the product labeling.

Additionally, setbacks may be caused by new safety or efficacy observations made in clinical trials, including previously unreported adverse events. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA approval or European Commission authorization. If we fail to obtain positive results in our Phase 3 clinical trials of setmelanotide, the development timeline and regulatory approval and commercialization prospects for setmelanotide, and, correspondingly, our business and financial prospects would be materially adversely affected.

The number of patients suffering from each of the MC4 pathway deficiencies we are targeting is small and has not been established with precision. If the actual number of patients is smaller than we estimate, our revenue and ability to achieve profitability may be materially adversely affected.

Due to the rarity of our target indications, there is no comprehensive patient registry or other method of establishing with precision the actual number of patients with MC4 pathway deficiencies. As a result, we have had to rely on other available sources to derive prevalence estimates for our target indications. Since the published epidemiology studies for these genetic deficiencies are based on relatively small population samples, and are not amenable to robust statistical analyses, it is possible that these projections may significantly exceed the addressable population, particularly given the need to genotype patients to definitively confirm a diagnosis.

We have estimated the potential addressable patient populations with these MC4 pathway deficiencies based on the following sources and assumptions:

- *POMC Deficiency Obesity.* There are approximately 50 patients with POMC deficiency obesity noted in a series of published case reports, each mostly reporting a single or small number of patients. However, we believe our addressable patient population for this deficiency may be approximately 100 to 500 patients in the United States, and a comparable addressable patient population in Europe, as most of the reported cases are from a small number of academic research centers, and because genetic testing for POMC deficiency is often unavailable and currently is rarely performed. Based on discussions with experts in rare diseases, we also believe the number of diagnosed cases could increase several-fold with increased awareness of this deficiency and the availability of new treatments.
- *LepR Deficiency Obesity and POMC Heterozygous Deficiency Obesity.* Our addressable patient population estimate for LepR deficiency obesity is approximately 500 to 2,000 patients in the United States, and for POMC heterozygous deficiency obesity is approximately 4,000 patients in the United States, with a comparable addressable patient population for both indications in Europe. Our estimates are based on:
 - epidemiology studies on LepR deficiency and POMC heterozygous deficiency in small cohorts of patients comprised of children with severe obesity and adults with severe obesity who have a history of early onset obesity;
 - U.S. Census Bureau figures for adults and children, and Centers for Disease Control and Prevention, or CDC, prevalence numbers for severe adult obese patients (BMI greater than 40 kg/ m²) and for severe early onset obese children (99th percentile at ages two to 17 years old); and
 - with wider availability of genetic testing expected for LepR deficiency and POMC heterozygous deficiency and increased awareness of new treatments, our belief that up to 40% of patients with these disorders may eventually be diagnosed.

Using these sources and assumptions, we calculated our estimates for addressable populations by multiplying (x) our estimate of the number of patients comprised of children with severe obesity and our estimate of a projected number of adults with severe obesity who have a history of early onset obesity, (y) the estimated prevalence from epidemiology studies of approximately 1% for LepR deficiency and 2% for POMC heterozygous, and (z) our estimated diagnosis rate of up to 40%.

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- *Bardet-Biedl Syndrome.* Our addressable patient population estimate for Bardet-Biedl syndrome is approximately 1,500 to 2,500 patients in the United States based on:
 - Published prevalence estimates of one in 100,000 in North America, which projects to approximately 3,250 people in the United States. We believe the majority of these patients are addressable patients; and
 - We believe that with wider availability of genetic testing expected for Bardet-Biedl syndrome and increased awareness of new treatments, the number of patients diagnosed with this disorder will increase.
- *Alström Syndrome.* Our addressable patient population estimate for Alström syndrome is approximately 500 to 1,000 patients worldwide. This estimate is based on:
 - Published prevalence estimates of one in 1,000,000 in North America, which projects to approximately 325 people in the United States. We believe the majority of these patients are addressable patients; and
 - We believe that with wider availability of genetic testing expected for Alström syndrome and increased awareness of new treatments, the number of patients diagnosed with this disorder will increase.
- *POMC Epigenetic Disorders.* There is currently no epidemiology data that defines the prevalence of POMC epigenetic disorders.

We believe that the patient populations in the European Union are at least as large as those in the United States. However, we do not have comparable epidemiological data from the European Union and these estimates are therefore based solely on applying relative population percentages to the Company-derived estimates described above.

We are conducting additional clinical epidemiology studies to strengthen these prevalence projections. In parallel, we are also developing a patient registry for diagnosed patients with POMC deficiency and LepR deficiency which will further inform prevalence projections for these rare genetic orders.

Another method to estimate the size of these ultra-rare populations by genetic epidemiology is using newly available large genomic databases, containing full genome sequencing or exome sequencing. Ultra-rare orphan diseases are generally categorized as those that affect fewer than 20 patients per million. We have begun some substantial efforts with a series of such databases and/or collaborators. Much of our preliminary work has been with a database of approximately 140,000 genomes, which is representative of the U.S. population. These efforts generally are based on the prevalence of heterozygous mutations, as true null mutations are ultra-rare, and then standard scientific methods such as the Hardy-Weinberg equilibrium calculations, are applied to estimate the prevalence in the U.S. population. These methods make assumptions that may not be sufficiently robust for ultra-rare genetic disorders, and have the inherent variability of estimates for rare events. In addition, the databases currently available only provide limited clinical data, such as, age, weight and BMI, that would be needed to associate genetic defects with severe obesity. However, until these data are confirmed in further genetic epidemiology efforts in additional databases, we must continue to base our patient population estimates on clinical epidemiological information.

In addition, if any approval that we obtain is based on a narrower definition of these patient populations than we had anticipated, then the potential market for setmelanotide for these indications will be smaller than we originally believed. In either case, a smaller patient population in our target indications would have a materially adverse effect on our ability to achieve commercialization and generate revenues.

If the actual number of patients suffering from each of the MC4 pathway deficiencies we are targeting is smaller than we estimate or if any approval that we obtain is based on a narrower definition of these patient populations, including pediatric populations, our ability to recruit patients to our trials may be materially adversely affected.

If the actual number of patients with any of the MC4 pathway deficiencies we are targeting is lower than we believe, it may be difficult to recruit patients, and this may affect the timelines for the completion of clinical trials. If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could also be delayed or prevented.

The pediatric population is an important patient population for setmelanotide and our addressable patient population estimates include pediatric populations. However, it may be more challenging to conduct studies in this population, and to locate and enroll pediatric patients. Additionally, it may be challenging to ensure that pediatric or adolescent patients adhere to clinical trial protocols.

We currently are treating patients 12 years of age and older in our trials, but we aim to gain regulatory approval and labeling for patients six years of age and older. Accordingly, we have applied for permission from the FDA and other equivalent competent authorities in the EU member states to enroll these younger patients, aged six to 11, in our pivotal trials. However, there may be issues that preclude this approval including, but not limited to, potential disagreement on dose titration or delivery methods and suitability of patient reported outcomes in younger patients, as well as avoiding over-suppression of normal appetite in adolescents. In addition, the competent authorities in the EU member states may consider the polyethylene glycol vehicle in the product to carry additional risks in pediatric patients. We cannot guarantee that the FDA or other equivalent competent authorities in the EU member states will ultimately grant permission to enroll the younger pediatric patient population, nor can we predict whether they will require additional pre-clinical studies or estimate the timing for approval, if any, of including patients under 12 in our trials or for the use of setmelanotide for such patients at all. The inability to obtain permission from the FDA or other equivalent competent authorities in the EU member states to enroll these younger patients under age 12 may narrow our potential patient population such that we may experience delays in enrolling sufficient numbers of patients in our clinical trials. Furthermore, if the FDA or other equivalent competent authorities in the EU member states do not approve the enrollment of the younger patient population in clinical trials or does not approve the use of setmelanotide in this population, the product candidate will not be labeled for promotion for these patients, even if they approve an NDA for setmelanotide for patients 12 and older.

While we have no knowledge of competitors developing product candidates intended to treat MC4 pathway deficiencies, competitors may emerge. If that were to occur and competitors initiated clinical trials for product candidates that treat the same indications as setmelanotide, patients who would otherwise be eligible for our clinical trials may instead enroll in the clinical trials of our competitors' product candidates.

Patient enrollment is also affected by other factors including:

- the severity of the disease under investigation;
- the eligibility criteria for the clinical trial in question;
- the perceived risks and benefits of the product candidate under study;
- the success of efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays, could require us to abandon one or more clinical trials altogether and could delay or prevent our

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receipt of necessary regulatory approvals. Enrollment delays in our clinical trials may result in increased development costs for setmelanotide, which would cause the value of our company to decline and limit our ability to obtain additional financing.

Failures or delays in the commencement or completion of our planned clinical trials of setmelanotide could result in increased costs to us and could delay, prevent or limit our ability to generate revenue and continue our business.

We completed Phase 2 clinical trials for setmelanotide in 2016 for POMC deficiency obesity and are currently enrolling Phase 3 clinical trials for setmelanotide for POMC deficiency obesity in 2017. We completed Phase 2 clinical trials for setmelanotide for LepR deficiency obesity, and we expect to enroll the first patient in our LepR deficiency obesity Phase 3 clinical trial in the second half of 2017. We have also initiated Phase 2 clinical trials for Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders. Successful completion of such clinical trials is a prerequisite to submitting an NDA to the FDA, a marketing authorization application to the EMA, and other applications for marketing authorization to equivalent competent authorities in foreign jurisdictions, and consequently, the ultimate approval and commercial marketing of setmelanotide. We do not know whether our planned additional Phase 2 or Phase 3 clinical trials will begin or whether any of our clinical trials will be completed on schedule, if at all, as the commencement and completion of clinical trials can be delayed or prevented for a number of reasons, including but not limited to:

- the FDA or other equivalent competent authorities in foreign jurisdictions may deny permission to proceed with our planned Phase 3 clinical trials or any other clinical trials we may initiate, or may place a clinical trial on hold;
- delays in filing or receiving approvals or additional investigational new drug application, or IND, that may be required;
- negative results from our ongoing and planned preclinical studies, or the FDA or other equivalent competent authorities in foreign jurisdictions requiring additional preclinical studies;
- delays in commencing additional necessary preclinical studies, including carcinogenicity and juvenile toxicology studies;
- delays in reaching or failing to reach agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- since many already diagnosed patients are at academic sites, delays in conducting clinical trials at academic sites due to the particular challenges and delays typically associated with those sites;
- inadequate quantity or quality of setmelanotide or other materials necessary to conduct clinical trials, including delays in the manufacturing of sufficient supply of finished drug product;
- difficulties obtaining Institutional Review Board, or IRB, and/or ethics committee approval to conduct a clinical trial at a prospective site or sites;
- challenges in recruiting and enrolling patients to participate in clinical trials, including the size and nature of the patient population, the proximity of patients to clinical trial sites, eligibility criteria for the clinical trial, the nature of the clinical trial protocol, the availability of approved effective treatments for the relevant disease and competition from other clinical trial programs for similar indications;
- severe or unexpected drug-related side effects experienced by patients in a clinical trial, including side effects previously identified in our completed clinical trials;
- delays in identifying and recruiting patients with any of the genetic causes of obesity in indications that we are targeting;

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- disagreement by the FDA, other regulatory agencies or the equivalent competent authorities in foreign jurisdictions with our clinical trial designs, which may in turn cause delays in initiating our clinical trials, or may lead to rejection of our interpretation of data from clinical trials or to changes in the requirements for approval even after it has reviewed and commented on the design for our clinical trials;
- the requirement to have a placebo controlled study even though the FDA and EMA did not impose one for POMC deficiency obesity, as we cannot be certain that this will be true for other indications or that the FDA or EMA, an advisory committee or the equivalent competent authorities in foreign jurisdictions will not change its guidance, as it has done so in the past for other open control trials;
- uncertainty related to the length of placebo-controlled intervals in clinical trials;
- the need to perform non-inferiority trials, which can be larger, longer and more costly, if treatment is approved for similar indications;
- potential delays in the initiation of our clinical trials of LepR deficiency obesity due to the fact that we have not yet had discussions with the FDA regarding clinical trials for LepR deficiency obesity and, accordingly, do not know if the FDA will disagree with our clinical trial design;
- POMC heterozygous deficiency may have additional challenges, including that the FDA the EMA, or the equivalent competent authorities in foreign jurisdictions may require that we show that setmelanotide works better in these patients than in the genetically normal population; other challenges associated with these patients may include additional delays in initiating clinical trials for this indication due to uncertainty about the subset of these patients who will respond effectively to setmelanotide and the lack of discussion for this indication with the FDA;
- reports from preclinical or clinical testing of other weight loss therapies may raise safety or efficacy concerns; and
- difficulties retaining patients who have enrolled in a clinical trial but may be prone to withdraw due to rigors of the clinical trial, lack of efficacy, side-effects, personal issues or loss of interest.

Clinical trials may also be delayed or terminated as a result of ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, the FDA or other equivalent competent authorities in foreign jurisdictions, the IRBs or ethics committees at the sites where the IRBs or the ethics committees are overseeing a clinical trial, a data and safety monitoring board, or DSMB, or Safety Monitoring Committee, or SMC, overseeing the clinical trial at issue or other equivalent competent authorities due to a number of factors, including, among others:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical trial protocols;
- inspection of the clinical trial operations or trial sites by the FDA or other equivalent competent authorities that reveals deficiencies or violations that require us to undertake corrective action, including the imposition of a clinical hold;
- unforeseen safety issues, adverse side effects or lack of effectiveness;
- changes in government regulations or administrative actions;
- problems with clinical trial supply materials; and
- lack of adequate funding to continue the clinical trial.

Changes in regulatory requirements, FDA or EMA guidance or unanticipated events during our clinical trials of setmelanotide may occur, which may result in changes to clinical trial protocols, changes to instruments for measuring subjective systems or additional clinical trial requirements, which could result in increased costs to us and could delay our development timeline.

Changes in regulatory requirements, FDA guidance, guidance published by the EMA or the other competent authorities in foreign jurisdictions, or unanticipated events during our clinical trials may force us to amend clinical trial protocols or the FDA, or the other competent authorities in foreign jurisdictions may impose additional clinical trial requirements. For instance, the FDA issued draft guidance on developing products for weight management in February 2007. In March 2012, the FDA's Endocrinologic and Metabolic Drugs Advisory Committee met to discuss possible changes to how the FDA evaluates the cardiovascular safety of weight-management drugs, and the FDA may require additional studies to support registration. In addition, the FDA is considering broader applicability of requirements for cardiovascular outcomes trials, or CVOTs, presenting the possibility of cardiovascular risk pre-approval, including for obesity products. While our Phase 3 discussions with the FDA have not resulted in a requirement for any of these activities, any future requirement for these activities could result in additional clinical requirements for setmelanotide, increase our costs and delay approval of setmelanotide.

Amendments to our clinical trial protocols would require resubmission to the FDA and IRBs or other competent authorities and ethics committees in foreign jurisdictions for review and approval, which may adversely impact the cost, timing or successful completion of a clinical trial. If we experience delays completing, or if we terminate, any of our clinical trials, or if we are required to conduct additional clinical trials, the commercial prospects for setmelanotide may be harmed and our ability to generate product revenue will be delayed.

In addition, as part of commencing our Phase 3 clinical trial for setmelanotide in POMC deficiency obesity, we sought FDA concurrence with, and received substantial input on, the use of Patient Reported Outcome, or PRO, and Observer Reported Outcome, or ORO questionnaires for measuring subjective endpoints for changes in hunger and/or food-seeking behavior and compulsions. A PRO is a measurement based on a report that comes from the patient about the status of a patient's health condition, without amendment or interpretation of the patient's response by a clinician or anyone else. An ORO is a measurement based on an observation by someone other than the patient or a health professional, such as a parent, spouse or other non-clinical caregiver who is in a position to regularly observe and report on a specific aspect of the patient's health. In our Phase 3 clinical trial for setmelanotide, based on the FDA feedback, we plan to measure the ability of setmelanotide to mitigate hunger and/or hyperphagia, the overriding physiological drive to eat, through PRO and ORO questionnaires. The questionnaires are designed to elicit feedback from patients on how well setmelanotide decreases their hunger, and from their family members or caregivers on the effect of setmelanotide on the patients' food seeking behavior.

To our knowledge, no sponsor of an approved drug has yet used PRO or ORO questionnaires to generate data on hyperphagia or hunger mitigating endpoints. Because we may be relying on clinical endpoints that have not previously been the subject of prior FDA approvals, there is a risk that the FDA or other equivalent competent authorities in foreign jurisdictions may not consider the endpoints to provide evidence of clinically meaningful results or that results may be difficult for the FDA to interpret, in particular for the pediatric age group. If we experience delays in our ongoing validation of our PRO or ORO questionnaires, or do not receive agreement with those proposed questionnaires based on the conceptual framework, content reliability, other measures of validity, or their ability to detect changes in hyperphagia or hunger, we may experience delays in our trials or in product approval as well as be unable to reference data on hyperphagia or hunger in our product labeling. Finally, our Phase 3 clinical trials will be assessing hunger using multiple methods, some of which were previously used in Phase 2, but some of which were initiated in Phase 3 trials and for which little data is available. Hence it is possible that the effects on hunger seen in Phase 2 trials may differ with some of the new methodologies for assessing hunger being used in Phase 3 trials, or may not support language in the proposed product labeling.

Setmelanotide may cause undesirable side effects that could delay or prevent regulatory approval, limit the commercial profile of an approved labeling, or result in significant negative consequences following marketing approval, if any.

First generation MC4R agonists were predominantly small molecules that failed in clinical trials due to significant safety issues, particularly increases in blood pressure, and had limited efficacy. Undesirable side effects caused by setmelanotide could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive labeling or the delay or denial of regulatory approval by the FDA or other equivalent competent authorities in foreign jurisdictions.

Setmelanotide is an MC4R agonist. Potential side effects of MC4R agonism, which have been noted either with setmelanotide or with other MC4R agonists in clinical trials and preclinical studies, may include:

- adverse effects on cardiovascular parameters, such as increases in heart rate and blood pressure;
- erections in males and similar effects in women, such as sexual arousal, clitoral swelling and hypersensitivity;
- nausea and vomiting;
- reduced appetite;
- effects on mood, depression, anxiety and other psychiatric manifestations; and
- other effects, specifically back pain, headaches, fatigue, diarrhea and joint pain, that have been seen numerically more frequently in setmelanotide-treated patients as compared with placebo patients.

Injection site reactions have been seen in subcutaneous, or SC injections with setmelanotide. In addition, setmelanotide has likely off-target effects on the closely-related MC1 receptor, which mediates tanning in response to sun exposure. Other MC1 mediated effects include darkening of skin blemishes, such as freckles and moles, and hair color change in one subject. These effects have generally been reversible in clinical trials, but it is still unknown if they will be reversible with long-term exposure. The MC1 mediated effects may also carry risks. The long-term impact of MC1 activation has not been tested in clinical trials, and could potentially include increases in skin cancer, excess biopsy procedures and cosmetic blemishes. These skin changes may also result in unblinding, which could make interpretation of clinical trial results more complex and possibly subject to bias.

The safety data we have disclosed to date represents our interpretation of the data at the time of disclosure and they are subject to our further review and analysis. The only serious adverse event possibly attributed to setmelanotide in our clinical trials was one report of atypical chest pain seen in our Phase 2 clinical trial with once daily SC injection, although there was no evidence of any serious respiratory or cardiac cause on careful examination. Overall, there have been five other serious adverse events in the overall clinical development program in addition to the serious adverse event described above: two others during treatment on setmelanotide, left arm numbness and influenza immunization reaction and three during treatment with placebo, including biliary dyskinesia, severe groin strain and pelvic inflammatory disease. None of these serious adverse events was considered related to setmelanotide.

We are also initiating trials of setmelanotide in potential new indications that include patients who might have more serious underlying conditions, such as Alström syndrome and lipodystrophy. It is possible that the underlying conditions in these patients, such as congestive heart failure and pancreatitis, may confound the understanding of the safety profile of setmelanotide.

In addition, our interpretation of the safety data from our clinical trials is contingent upon the review and ultimate approval of the FDA, other regulatory authorities or other equivalent competent authorities in foreign jurisdictions. The FDA or other equivalent competent authorities in foreign jurisdictions may

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not agree with our methods of analysis or our interpretation of the results. In addition, the long-term effects of setmelanotide have only been tested in a limited number of patients.

Further, if setmelanotide receives marketing approval and we or others identify undesirable side effects caused by the product, or any other similar product, before or after the approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may request that we withdraw the product from the market or may limit their approval of the product through labeling or other means;
- regulatory authorities may require the addition of labeling statements, such as a "boxed" warning or a contraindication;
- the FDA and other equivalent competent authorities in foreign jurisdictions may require the addition of a Risk Evaluation and Mitigation Strategy, or REMS, or other specific obligations as a condition for marketing authorization due to the need to limit treatment to rare patient populations, or to safety concerns;
- we may be required to change the way the product is distributed or administered, conduct additional clinical trials or change the labeling of the product;
- we may decide to remove the product from the marketplace;
- we could be sued and held liable for injury caused to individuals exposed to or taking the product; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of setmelanotide and could substantially increase the costs of commercializing setmelanotide and significantly impact our ability to successfully commercialize setmelanotide and generate revenues.

Although we have been granted orphan drug designation for setmelanotide in treating POMC deficiency obesity, we may be unable to obtain orphan drug designation for other uses or to obtain exclusivity in any use. Even with exclusivity, competitors may obtain approval for different drugs that treat the same indications as setmelanotide.

The FDA may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, or the Orphan Drug Act, the FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition, which is defined under the Federal Food, Drug and Cosmetic Act, or FDCA, as having a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States.

Generally, if a product candidate with an orphan drug designation receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of seven years of marketing exclusivity, which precludes the FDA from approving another marketing application for a product that constitutes the same drug treating the same indication for that marketing exclusivity period, except in limited circumstances.

The exclusivity period in the United States can be extended by six months if the NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. Even under these circumstances, we may not be granted pediatric approval from the FDA for these indications. Orphan drug exclusivity may be revoked if the FDA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition. Other potential benefits of orphan drug designation and/or approval of a designated drug include eligibility for: exemption from certain prescription drug user fees, tax credits for

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certain qualified clinical testing expenses, and waivers from the pediatric assessment requirements of the Pediatric Research Equity Act, or PREA.

Although we have been granted orphan drug designation for setmelanotide in treating POMC deficiency obesity, if we request orphan drug designation for setmelanotide for other uses, there can be no assurance that the FDA will grant such designation. For example, if the population of patients who would be appropriate candidates for a drug is 200,000 or more individuals, the drug may not qualify for orphan drug designation, even if the population for which the sponsor seeks approval is lower than 200,000. Additionally, the designation of setmelanotide as an orphan drug does not guarantee that the FDA will accelerate regulatory review of, or ultimately approve, setmelanotide.

Even if we obtain orphan drug exclusivity for setmelanotide, that exclusivity may not effectively protect setmelanotide from competition because different drugs can be approved for the same condition. In the United States, even after an orphan drug is approved, the FDA may subsequently approve another drug for the same condition if the FDA concludes that the latter drug is not the same drug or is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

On August 3, 2017, Congress passed the FDA Reauthorization Act of 2017, or the FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Although we have obtained breakthrough therapy designation for setmelanotide for the treatment of obesity associated with genetic defects upstream of the MC4 receptor in the leptin-melanocortin pathway, which includes both POMC deficiency obesity and LepR deficiency obesity, the FDA may rescind the breakthrough designation and we may be unable to obtain breakthrough therapy designation for other uses. In addition, breakthrough therapy designation by the FDA may not lead to a faster development, regulatory review or approval process, and it does not increase the likelihood that setmelanotide will receive marketing approval in the United States.

Under the Food and Drug Administration Safety and Innovation Act, or FDASIA, the FDA is authorized to give certain products "breakthrough therapy designation." Breakthrough therapy product candidate is defined as a product candidate that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that such product candidate may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. The FDA will seek to ensure the sponsor of breakthrough therapy product candidate receives intensive guidance on an efficient drug development program, intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review and a rolling review process whereby the FDA may consider reviewing portions of an NDA before the sponsor submits the complete application. Product candidates designated as breakthrough therapies by the FDA may be eligible for other expedited programs, such as priority review, if supported by clinical data.

Designation as breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe setmelanotide meets the criteria for designation as breakthrough therapy for other uses, the FDA may disagree. In any event, the receipt of breakthrough therapy designation for a product candidate, or acceptance for one or more of the FDA's other expedited programs, may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA

procedures and does not guarantee ultimate approval by the FDA. Additionally, the FDA may later decide that the product candidate no longer meets the conditions for designation and may withdraw designation at any time or decide that the time period for FDA review or approval will not be shortened.

We may not be able to translate the current formulations of setmelanotide for methods of delivery that would be acceptable to the FDA or other equivalent competent authorities in foreign jurisdictions or commercially successful.

Setmelanotide is currently administered by SC injection using small insulin-type needles. SC injection is generally less well-received by patients than other methods of administration, such as oral administration. Considerable additional resources and efforts, including potential studies, may be necessary in order to translate the current formulations of setmelanotide into forms that will be well-received by patients.

We have entered into a license agreement with Camurus AB, or Camurus, for the use of Camurus' drug delivery technology, FluidCrystal, to formulate setmelanotide. This formulation, if successfully developed for setmelanotide, will be delivered subcutaneously, similar to our current formulation, except that we anticipate it will be injected once weekly.

While we plan to utilize the current formulation, or to develop new and useful formulations and delivery technology for setmelanotide, we cannot estimate the probability of success, nor the resources and time needed to succeed. If we are unable to utilize this formulation, or to develop new formulations, setmelanotide may not achieve significant market acceptance and our business, financial condition and results of operations may be materially harmed.

Our approach to treating patients with MC4 pathway deficiencies requires the identification of patients with unique genetic subtypes, for example, POMC genetic deficiency. The FDA or other equivalent competent authorities in foreign jurisdictions could require the approval or CE mark of an in vitro companion diagnostic device to ensure appropriate selection of patients as a condition of approving setmelanotide. The development and approval or CE mark of an in vitro companion diagnostic device would require substantial financial resources and could delay regulatory approval of setmelanotide.

We intend to focus our development of setmelanotide as a treatment for obesity caused by certain genetic deficiencies affecting the MC4 pathway. In order to assist in identifying this subset of patients, we employ a genetic diagnostic test, which is a test or measurement that evaluates the presence of genetic variants in a patient. The FDA has advised that for our clinical trial of setmelanotide to treat POMC deficiency obesity, it will be sufficient to use genetic diagnostic testing known as Sanger bi-directional nucleotide sequencing, as long as that testing is performed by laboratories meeting the standards of the Clinical Laboratory Improvement Amendments, or CLIA, for Laboratory Developed Tests, or LDTs. Currently the Centers for Medicare and Medicaid Services, or CMS, regulates LDTs and the laboratories that develop them, and enforces CLIA. CMS evaluates whether there is clinical utility for each specific test, and also performs postmarket oversight of laboratory operational processes. CMS coverage determinations of clinical utility measure the ability of the test to impact clinically meaningful health outcomes, such as mortality or morbidity, through the adoption of efficacious treatments. CMS's oversight through the CLIA program is designed to confirm that a lab assesses analytical validity, but does not confirm whether it had results from an analytical validity assessment that were sufficient to support the claimed intended use of the test. The FDA has issued guidance indicating, however, that in the future it intends to assert jurisdiction over LDTs and to increase regulatory requirements for LDTs. If the FDA does so, the burdens and costs of using LDTs to select patients for setmelanotide could increase, the availability of those LDTs could be negatively affected, and our development program for setmelanotide could be delayed, which in turn could delay or impair our ability to proceed to commercialization.

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Although the FDA has advised us that an LDT is sufficient for identifying patients in our clinical trials, the agency also indicated that approval of an *in vitro* companion diagnostic device may be necessary should clinical results reveal that genetic testing is needed for the safe use of setmelanotide, such as to avoid significant toxicities in certain patients or because the drug might provide only marginal benefits except in a very clearly defined eligible population. *In vitro* companion diagnostic devices provide information that is essential for the safe and effective use of a corresponding therapeutic product. These companion diagnostic devices may be co-developed with a device manufacturer or with a laboratory, and generally require FDA approval as well.

Should the FDA or other equivalent competent authorities in foreign jurisdictions require the use of a companion diagnostic device, we may face significant delays or obstacles in obtaining approval of an NDA, or of comparable foreign marketing authorization for setmelanotide as the FDA or other equivalent competent authorities in foreign jurisdictions may take the position that a companion diagnostic is required prior to granting approval of setmelanotide. In addition, we may be dependent on the sustained cooperation and effort of third-party collaborators with whom we may partner in the future to develop *in vitro* companion diagnostic devices. We and our potential future collaborators may encounter difficulties in developing such tests, including issues relating to the selectivity and/or specificity of the diagnostic, analytical validation, reproducibility or clinical validation. Any delay or failure by us or our potential future collaborators to develop or obtain regulatory clearance or approval of, or to CE mark, such tests, if necessary, could delay or prevent approval of setmelanotide.

If the FDA deems setmelanotide to require an *in vitro* companion diagnostic device to accurately identify the patients who belong to the target subset, the FDA will require product labeling that limits use to only those patients who express the genetic variants identified by the device. Moreover, even if setmelanotide and an *in vitro* companion diagnostic device are approved together, the device itself may be subject to reimbursement limitations that could limit access to treatment and therefore adversely affect our business and financial results.

We have only one product candidate and we may not be successful in any future efforts to identify and develop additional product candidates.

We have only one product candidate and may seek to identify and develop additional product candidates, both within and outside of our current area of expertise. If so, the success of our business may depend primarily on our ability to identify, develop and commercialize these products. Research programs to identify new product candidates require substantial technical, financial and human resources. We may fail to identify other potential product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. In addition, any such efforts could adversely impact our continued development and commercialization of setmelanotide.

If any of these events occur, we may be forced to abandon some or all of our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations.

Prader-Willi syndrome, or PWS, is a complex disease, and companies have had difficulties in developing new therapies for PWS.

Although we have been granted orphan drug designation for setmelanotide in treating PWS, we are not moving directly towards a Phase 3 trial in PWS at this time, but instead will be assessing how to proceed in another Phase 2 trial. We do not know the probability that we will be able to proceed to Phase 3

and/or approval, even when these efforts are completed. In addition, the experience by others suggests that PWS patients are high risk for adverse experiences and hence clinical trials in that population are extremely challenging. It may be both difficult to determine if adverse effects in this population are due to the disease, setmelanotide or some combination of both. PWS is a complex multigenic disease, and the hypothesis that PWS is an upstream MC4 pathway disorder is supported primarily on the role of only one of those genes, MAGEL2, in animal models of obesity. Our results may support that PWS is not an upstream MC4 pathway disorder. Alternatively, other design factors may have influenced the outcome of this trial, and we will be reassessing in 2018 the possibility of future Phase 2 trials in PWS that address the following potential factors: duration of treatment, younger age of population, improved setmelanotide pharmacokinetics, consideration of higher doses, and operational limitations of the completed Phase 2 trial. There can be no assurances that some of the factors that affected the results of the PWS trials will not also adversely impact the results of our trials for other indications.

Risks Related to the Commercialization of Setmelanotide

Even if approved, reimbursement policies could limit our ability to sell setmelanotide.

Market acceptance and sales of setmelanotide will depend on reimbursement policies and may be affected by healthcare reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels for those medications. Cost containment is a primary concern in the U.S. healthcare industry and in foreign jurisdictions. Government authorities and these third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. We cannot be sure that reimbursement will be available for setmelanotide and, if reimbursement is available, the level of such reimbursement. Reimbursement may impact the demand for, or the price of setmelanotide. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize setmelanotide.

In some foreign countries, particularly in Canada and in the EU member states, the pricing of prescription pharmaceuticals is subject to strict governmental control. In these countries, pricing negotiations with governmental authorities can take six to 12 months or longer after the receipt of regulatory approval and product launch. To obtain favorable reimbursement for the indications sought or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of setmelanotide with other available therapies. If reimbursement for setmelanotide is unavailable in any country in which we seek reimbursement, if it is limited in scope or amount, if it is conditioned upon our completion of additional clinical trials or if pricing is set at unsatisfactory levels, our operating results could be materially adversely affected.

In the European Union, in particular, each EU member state can restrict the range of medicinal products for which its national health insurance system provides reimbursement and can control the prices of medicinal products for human use marketed in its territory. As a result, following receipt of marketing authorization in an EU member state, through any application route, an applicant is required to engage in pricing discussions and negotiations with the competent pricing authority in the individual EU member states. Some EU member states operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed upon. Other EU member states approve a specific price for the medicinal product or may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. The downward pressure on healthcare costs in general, particularly prescription drugs, has become more intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, we may face competition for setmelanotides from lower priced products in foreign countries that have placed price controls on pharmaceutical products.

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Health Technology Assessment, or HTA, of medicinal products, however, is becoming an increasingly common part of the pricing and reimbursement procedures in some EU member states, including the United Kingdom, France, Germany, Ireland, Italy and Sweden. HTA is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. HTA generally focuses on the clinical efficacy and effectiveness, safety, cost, and cost-effectiveness of individual medicinal products as well as their potential implications for the healthcare system. Those elements of medicinal products are compared with other treatment options available on the market. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU member states. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product varies between EU member states. In addition, pursuant to Directive 2011/24/EU on the application of patients' rights in cross-border healthcare, a voluntary network of national authorities or bodies responsible for HTA in the individual EU member states was established. The purpose of the network is to facilitate and support the exchange of scientific information concerning HTAs. This may lead to harmonization of the criteria taken into account in the conduct of HTAs between EU member states and in pricing and reimbursement decisions and may negatively affect price in at least some EU member states.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell setmelanotide, if approved, we may not be able to generate any revenue.

We do not currently have infrastructure in place for the sale, marketing or distribution of pharmaceutical products. In order to market setmelanotide, if approved by the FDA or other equivalent competent authorities in foreign jurisdictions, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, or if we are unable to do so on commercially reasonable terms, our business, results of operations, financial condition and prospects would be materially adversely affected.

Even if we receive marketing approval for setmelanotide in the United States, we may never receive regulatory approval to market setmelanotide outside of the United States.

We intend to pursue marketing approval for setmelanotide in the European Union and in other countries worldwide. In order to market any product outside of the United States, we must establish and comply with the numerous and varying safety, efficacy and other regulatory requirements of other countries. Approval procedures vary among countries and can involve additional setmelanotide testing and additional administrative review periods. The time required to obtain approvals in other countries might differ from that required to obtain FDA approval. The marketing approval processes in other countries may implicate all of the risks detailed above regarding FDA approval in the United States as well as other risks. In particular, in many countries outside of the United States, products must receive pricing and reimbursement approval before the product can be commercialized. Obtaining this approval can result in substantial delays in bringing products to market in such countries. Marketing approval in one country does not ensure marketing approval in another, but a failure or delay in obtaining marketing approval in one country may have a negative effect on the regulatory process or commercial activities in others. Failure to obtain marketing approval in other countries or any delay or other setback in obtaining such approval would impair our ability to market setmelanotide in such foreign markets. Any such impairment would reduce the size of our potential market share and could have a material adverse impact on our business, results of operations and prospects.

Even if we receive marketing approval for setmelanotide, we may not achieve market acceptance, which would limit the revenue that we generate from the sale of setmelanotide.

The commercial success of setmelanotide, if approved by the FDA or other equivalent competent authorities in foreign jurisdictions, will also depend upon the awareness and acceptance of setmelanotide within the medical community, including physicians, patients and third-party payors. If setmelanotide is approved but does not achieve an adequate level of acceptance by patients, physicians and third-party payors, we may not generate sufficient revenue to become or remain profitable. Before granting reimbursement approval, third-party payors may require us to demonstrate that, in addition to treating obesity caused by certain genetic deficiencies affecting the MC4 pathway, setmelanotide also provides incremental health benefits to patients. Our efforts to educate the medical community and third-party payors about the benefits of setmelanotide may require significant resources and may never be successful. All of these challenges may impact our ability to ever successfully market and sell setmelanotide.

Market acceptance of setmelanotide, if approved, will depend on a number of factors, including, among others:

- the ability of setmelanotide to treat obesity caused by certain genetic deficiencies affecting the MC4 pathway and, if required by any competent authority in connection with the approval for these indications, to provide patients with incremental health benefits, as compared with other available treatments, therapies, devices or surgeries;
- the relative convenience and ease of SC injections as the necessary method of administration of setmelanotide, including as compared with other treatments for obese patients;
- the prevalence and severity of any adverse side effects associated with setmelanotide;
- limitations or warnings contained in the labeling approved, as well as the existence of a REMS, for setmelanotide by the FDA or the specific obligations imposed as a condition for marketing authorization imposed by other equivalent competent authorities in foreign jurisdictions, particularly by the European Commission;
- availability of alternative treatments, including a number of obesity therapies already approved or expected to be commercially launched in the near future;
- the size of the target patient population, and the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the ability of setmelanotide to treat the maximum range of pediatric patients, and any limitations on its indications for use, such as if the labeling limits the approved population to patients ages 12 and above;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning setmelanotide or competing products and treatments;
- pricing and cost effectiveness;
- the effectiveness of our sales and marketing strategies;
- our ability to increase awareness of setmelanotide through marketing efforts;
- our ability to obtain sufficient third-party coverage or reimbursement;
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage; and
- the likelihood that the FDA or other equivalent competent authorities in foreign jurisdictions may require development of a REMS as a condition of approval or post-approval, may not agree with

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our proposed REMS or may impose additional requirements that limit the promotion, advertising, distribution or sales of setmelanotide.

Our industry is intensely competitive. If we are not able to compete effectively against current and future competitors, we may not be able to generate revenue from the sale of setmelanotide, our business will not grow and our financial condition and operations will suffer.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We have competitors in a number of jurisdictions, many of which have substantially greater name recognition, commercial infrastructures and financial, technical and personnel resources than we have. Established competitors may invest heavily to quickly discover and develop compounds that could make setmelanotide obsolete or uneconomical. Any new product that competes with an approved product may need to demonstrate compelling advantages in efficacy, convenience, tolerability and safety to be commercially successful. Other competitive factors, including generic competition, could force us to lower prices or could result in reduced sales. In addition, new products developed by others could emerge as competitors to setmelanotide. If we are not able to compete effectively against our current and future competitors, our business will not grow and our financial condition and operations will suffer.

Currently, there are no approved or effective current treatments for regulating hunger and hyperphagia related behaviors of patients with POMC deficiency obesity, LepR deficiency obesity, Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, or POMC epigenetic disorders. Bariatric surgery is not a treatment option for these genetic disorders of obesity because the severe obesity and hyperphagia associated with these disorders are considered to be risk factors for bariatric surgery. While we are unaware of any competitive products in development for the obesity and hyperphagia caused by MC4 pathway deficiencies specifically, new competitors may emerge which could limit our business opportunity in the future.

We face potential product liability exposure, and, if claims are brought against us, we may incur substantial liability.

The use of setmelanotide in clinical trials and the sale of setmelanotide, if approved, exposes us to the risk of product liability claims. Product liability claims might be brought against us by patients, healthcare providers or others selling or otherwise coming into contact with setmelanotide. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design or a failure to warn of dangers inherent in the product, including as a result of interactions with alcohol or other drugs, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection laws. If we become subject to product liability claims and cannot successfully defend ourselves against them, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in, among other things:

- withdrawal of patients from our clinical trials;
- substantial monetary awards to patients or other claimants;
- decreased demand for setmelanotide or any future product candidates following marketing approval, if obtained;
- damage to our reputation and exposure to adverse publicity;
- litigation costs;
- distraction of management's attention from our primary business;
- loss of revenue; and

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- the inability to successfully commercialize setmelanotide or any future product candidates, if approved.

We maintain product liability insurance coverage for our clinical trials with a \$10.0 million annual aggregate coverage limit. Our insurance coverage may be insufficient to reimburse us for any expenses or losses we may suffer. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses, including if insurance coverage becomes increasingly expensive. If and when we obtain marketing approval for setmelanotide, we intend to expand our insurance coverage to include the sale of commercial products. However, we may not be able to obtain this product liability insurance on commercially reasonable terms. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. The cost of any product liability litigation or other proceedings, even if resolved in our favor, could be substantial, particularly in light of the size of our business and financial resources. A product liability claim or series of claims brought against us could cause our stock price to decline and, if we are unsuccessful in defending such a claim or claims and the resulting judgments exceed our insurance coverage, our financial condition, business and prospects could be materially adversely affected.

Risks Related to Our Dependence on Third Parties

We rely, and expect that we will continue to rely, on third parties to conduct clinical trials for setmelanotide. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize setmelanotide and our business could be substantially harmed.

We enter into agreements with third-party CROs to provide monitors for and to manage data for our ongoing clinical trials. We rely heavily on these parties for the execution of clinical trials for setmelanotide and control only certain aspects of their activities. As a result, we have less direct control over the conduct, timing and completion of these clinical trials and the management of data developed through the clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. However, we remain responsible for the conduct of these trials and are subject to enforcement which may include civil and criminal liabilities for any violations of FDA rules and regulations and the comparable foreign regulatory provisions during the conduct of our clinical trials. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- devote inadequate resources to our clinical trials;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form more favorable relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our clinical trials and may subject us to unexpected cost increases that are beyond our control. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with current Good Clinical Practices, or cGCPs, which are guidelines enforced by the FDA, the Competent Authorities of the EU member states and equivalent competent authorities in foreign jurisdictions for any products in clinical development. The FDA enforces these regulations and cGCP guidelines through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we or our CROs fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or other equivalent competent authorities in foreign jurisdictions may require us to perform additional clinical trials before

approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our clinical trials comply with cGCPs. In addition, our clinical trials must be conducted with products produced under current Good Manufacturing Practices, or cGMPs. Our failure or the failure of our CROs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action up to and including civil and criminal penalties.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain are compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any such clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize, setmelanotide. As a result, our financial results and the commercial prospects for setmelanotide in the subject indication would be harmed, our costs could increase and our ability to generate revenue could be delayed.

We rely completely on third-party suppliers to manufacture our clinical drug supplies of setmelanotide, and we intend to rely on third parties to produce commercial supplies of setmelanotide and preclinical, clinical and commercial supplies of any future product candidate.

We do not currently have, nor do we plan to acquire, the infrastructure or capability to internally manufacture our clinical drug supply of setmelanotide, or any future product candidates, for use in the conduct of our preclinical studies and clinical trials, and we lack the internal resources and the capability to manufacture any product candidate on a clinical or commercial scale. The facilities used by our contract manufacturing organizations, or CMOs, to manufacture the active pharmaceutical ingredient, or API, and final drug product must pass inspection by the FDA and other equivalent competent authorities in foreign jurisdictions pursuant to inspections that would be conducted after we submit our NDAs or relevant foreign regulatory submission to the other equivalent competent authorities in foreign jurisdictions. In addition, our clinical trials must be conducted with products produced under cGMP regulations. Our failure or the failure of our CROs or CMOs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action, including civil and criminal penalties. If we import any drugs or drug substances, we would be subject to FDA and U.S. Bureau of Customs and Border Patrol, or CBP, import regulation requirements. Such enforcement for our failure or our CROs or CMOs' failure to comply with these regulations could result in import delays, detention of products, and, depending on criteria such as the history of violative activities, the FDA could place a foreign firm or certain drug substances or products on Import Alert and require that all such drug substances or products be subject to detention without physical examination, or DWPE, which could significantly impact the global supply chain for setmelanotide. FDARA provides that prescription drug products, with the exception of those on the FDA's drug shortage list or properly imported by individuals, may not be imported for commercial use if they were manufactured in a foreign country, unless they have been approved or are otherwise authorized to be marketed in the United States and are labeled accordingly.

We currently contract with a third party for the manufacture of setmelanotide and intend to continue to do so in the future. We have entered into a process development and manufacturing services agreement with Corden Pharma Brussels S.A, or Corden, formerly Peptisyntha SA prior to its acquisition by Corden, under which Corden will provide certain process development and manufacturing services in connection with the manufacture of setmelanotide. We have also entered into a process development and manufacturing services agreement with Recipharm Monts S.A.S, or Recipharm, under which Recipharm will provide certain process development and manufacturing services in connection with the manufacture of setmelanotide. Under our agreements, we pay both Corden and Recipharm for services in accordance with the terms of mutually agreed upon work orders, which we, Corden and Recipharm may enter into

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from time to time. The agreement with Corden also provides that, subject to certain conditions, for a period following each product launch date, we will source from Corden a portion of our requirements for that product being sourced from non-affiliate third parties. We may need to engage additional third-party suppliers to manufacture our clinical drug supplies. In the future, if we approach commercialization of setmelanotide or any future product candidate, we will need to engage other third parties to assist in, among other things, labeling, packaging, distribution, post-approval safety reporting, and pharmacovigilance activities. We cannot be certain that we can engage third-party suppliers on terms as favorable as those that are currently in place.

We do not perform the manufacturing of any drug products, and are completely dependent on, our CMOs to comply with cGMPs for manufacture of both API and finished drug product. We recognize that we are ultimately responsible for ensuring that our drug substances and finished product are manufactured in accordance with cGMPs, and, therefore, the company's management practices and oversight, including routine auditing, are critical. If our CMOs cannot successfully manufacture material that conform to our specifications and the strict regulatory requirements of the FDA or other equivalent competent authorities in foreign jurisdictions, they may be subject to administrative and judicial enforcement for non-compliance and the drug products would be deemed misbranded or adulterated and prohibited from distribution into interstate commerce. Furthermore, all of our CMOs are engaged with other companies to supply and/or manufacture materials or products for such companies, which exposes our manufacturers to regulatory risks for the production of such materials and products. As a result, failure to satisfy the regulatory requirements for the production of those materials and products may affect the regulatory clearance of our CMOs' facilities generally. If the FDA or another equivalent competent foreign regulatory agency does not approve these facilities for the manufacture of setmelanotide or if it withdraws its approval in the future, we may need to find alternative manufacturing facilities, which would adversely impact our ability to develop, obtain regulatory approval for or market setmelanotide.

We are currently in the process of manufacturing finished drug product for use in our upcoming clinical trials. We believe we currently have a sufficient amount of finished setmelanotide, diluent and placebo to complete our planned clinical trials. However, these projections could change based on delays encountered with manufacturing activities, equipment scheduling and material lead times. Any such delays in the manufacturing of finished drug product could delay our planned clinical trials of setmelanotide, which could delay, prevent or limit our ability to generate revenue and continue our business.

We do not have long-term supply agreements in place with our contractors, and each batch of setmelanotide is individually contracted under a quality and supply agreement. If we engage new contractors, such contractors must be approved by the FDA and other equivalent competent authorities in foreign jurisdictions. We will need to submit information to the FDA and other equivalent competent authorities in foreign jurisdictions describing the manufacturing changes. If manufacturing changes occur post-approval, the FDA will have to approve these changes. We plan to continue to rely upon CMOs and, potentially, collaboration partners to manufacture commercial quantities of setmelanotide, if approved. Our current scale of manufacturing appears adequate to support all of our current needs for clinical trial supplies for setmelanotide. If setmelanotide is approved, we will need to identify CMOs or partners to produce setmelanotide on a larger scale.

Risks Related to Our Intellectual Property Rights

If we are unable to adequately protect our proprietary technology or maintain issued patents that are sufficient to protect setmelanotide, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.

Our commercial success will depend in part on our success in obtaining and maintaining issued patents and other intellectual property rights in the United States and elsewhere and protecting our proprietary technology. If we do not adequately protect our intellectual property and proprietary technology, competitors may be able to use our technologies and erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability.

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We cannot provide any assurances that any of our patents have, or that any of our pending patent applications that mature into issued patents will include, claims with a scope sufficient to protect setmelanotide. Other parties have developed technologies that may be related or competitive to our approach, and may have filed or may file patent applications and may have received or may receive patents that may overlap with our patent applications, either by claiming the same methods or formulations or by claiming subject matter that could dominate our patent position. The patent positions of biotechnology and pharmaceutical companies, including our patent position, involve complex legal and factual questions, and, therefore, the issuance, scope, validity and enforceability of any patent claims that we may obtain cannot be predicted with certainty.

Although an issued patent is presumed valid and enforceable, its issuance is not conclusive as to its validity or its enforceability and such patent may not provide us with adequate proprietary protection or competitive advantages against competitors with similar products. Patents, if issued, may be challenged, deemed unenforceable, invalidated or circumvented. U.S. patents and patent applications or the patents and patent application obtained or submitted pursuant to comparable foreign laws, may also be subject to interference proceedings, *ex parte* reexamination, *inter partes* review proceedings, post-grant review proceedings, supplemental examination and challenges in district court. Patents may be subjected to opposition or comparable proceedings lodged in various foreign, both national and regional, patent offices. These proceedings could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. In addition, such proceedings may be costly. Thus, any patents that we may own or exclusively license may not provide any protection against competitors. Furthermore, an adverse decision in an interference proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market or otherwise commercialize setmelanotide.

Competitors may also be able to design around our patents. Other parties may develop and obtain patent protection for more effective technologies, designs or methods. The laws of some foreign countries do not protect our proprietary rights to the same extent as the laws of the United States, and we may encounter significant problems in protecting our proprietary rights in these countries. If these developments were to occur, they could have a material adverse effect on our sales.

In addition, proceedings to enforce or defend our patents could put our patents at risk of being invalidated, held unenforceable or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. If any of our patents covering setmelanotide are invalidated or found unenforceable, our financial position and results of operations would be materially and adversely impacted. In addition, if a court found that valid, enforceable patents held by third parties covered setmelanotide, our financial position and results of operations would also be materially and adversely impacted.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- any of our patents, or any of our pending patent applications, if issued, will include claims having a scope sufficient to protect setmelanotide;
- any of our pending patent applications will issue as patents;
- we will be able to successfully commercialize setmelanotide, if approved, before our relevant patents expire;
- we were the first to make the inventions covered by each of our patents and pending patent applications;
- we were the first to file patent applications for these inventions;
- others will not develop similar or alternative technologies that do not infringe our patents;

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- any of our patents will be found to ultimately be valid and enforceable;
- any patents issued to us will provide a basis for an exclusive market for our commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties;
- we will develop additional proprietary technologies or product candidates that are separately patentable; or
- our commercial activities or products will not infringe upon the patents of others.

We rely upon unpatented trade secrets, unpatented know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with employees, consultants, collaborators and vendors. We also have agreements with employees and selected consultants that obligate them to assign their inventions to us. It is possible that technology relevant to our business will be independently developed by a person who is not a party to such an agreement. We may not be able to prevent the unauthorized disclosure or use of our technical knowledge or trade secrets by consultants, collaborators, vendors, former employees and current employees. Furthermore, if the parties to our confidentiality agreements breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets through such breaches or violations. Further, our trade secrets could otherwise become known or be independently discovered by our competitors.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming and divert the attention of our management and key personnel from our business operations. Even if we prevail in any lawsuits that we initiate, the damages or other remedies awarded may not be commercially meaningful. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid, is unenforceable and/or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing setmelanotide, if approved.

Our success will depend in part on our ability to operate without infringing the intellectual property and proprietary rights of third parties. We cannot assure you that our business, products and methods do not or will not infringe the patents or other intellectual property rights of third parties. For example, numerous third-party U.S. and non-U.S. patents and pending applications exist that cover melanocortin receptor analogs and methods of using these analogs.

The pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may allege that setmelanotide or the use of our technologies infringes patent claims or other intellectual property rights held by them or that we are employing their proprietary technology without authorization. For example, we received a letter in January 2013 from a third party bringing to our attention several patents and patent applications, both U.S. and non-U.S. We responded in April 2013 and have not received any further correspondence since then. Although most of the patents and patent applications mentioned in the letter were abandoned or not in force at the time the letter was sent to us, and subsequent to our response, the third party has allowed three additional U.S. patents to lapse for non-payment of patent maintenance fees, we cannot assure you that the holder of these third-party patents will not attempt to assert these patents against us.

Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. Any claim relating to intellectual property infringement that is successfully asserted against us may require us to pay substantial damages, including treble damages and attorney's fees if we are found to be willfully infringing another party's patents, for past use of the asserted intellectual property and royalties and other consideration going forward if we are forced to take a license. In addition, if any such claim were successfully asserted against us and we could not obtain such a license, we may be forced to stop or delay developing, manufacturing, selling or otherwise commercializing setmelanotide.

If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court, or redesign our products. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion.

In addition, in order to avoid infringing the intellectual property rights of third parties and any resulting intellectual property litigation or claims, we could be forced to do one or more of the following, which may not be possible and, even if possible, could be costly and time-consuming:

- cease development and commercialization of setmelanotide;
- pay substantial damages for past use of the asserted intellectual property;
- obtain a license from the holder of the asserted intellectual property, which license may not be available on reasonable terms, if at all; and
- in the case of trademark claims, rename setmelanotide.

Any of these risks coming to fruition could have a material adverse effect on our business, results of operations, financial condition and prospects.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as

exclusive ownership of, or right to use, such intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The U.S. Patent and Trademark Office, or U.S. PTO, and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

Issued patents covering setmelanotide could be found invalid or unenforceable if challenged in court.

If we or one of our licensing partners threatened or initiated legal proceedings against a third party to enforce a patent covering setmelanotide, the defendant could claim that the patent covering setmelanotide is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any one of several statutory requirements, including novelty, non-obviousness and enablement. Grounds for unenforceability assertions include allegations that someone connected with prosecution of the patent withheld material information from the U.S. PTO, or made a misleading statement, during patent prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, *inter partes* review, post grant review and equivalent proceedings in foreign jurisdictions, for example, opposition proceedings. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover setmelanotide or competitive products. The outcome following legal assertions of invalidity and/or unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on setmelanotide. Such a loss of patent protection would have a material adverse impact on our business.

We do not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing, prosecuting and defending patents on setmelanotide in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our product and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection,

particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. For example, an April 2017 report from the Office of the United States Trade Representative identified a number of countries, including India and China, where challenges to the procurement and enforcement of patent rights have been reported. Several countries, including India and China, have been listed in the report every year since 1989. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

We are dependent on licensed intellectual property. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing setmelanotide, if approved.

We have licensed our rights to setmelanotide from Ipsen Pharma SAS, or Ipsen. Our license with Ipsen imposes various obligations on us, and provides Ipsen the right to terminate the license in the event of our material breach of the license agreement, our failure to initiate or complete development of a licensed product, or our commencement of an action seeking to have an Ipsen licensed patent right declared invalid. Termination of our license from Ipsen would result in our loss of the right to use the licensed intellectual property, which would materially adversely affect our ability to develop and commercialize setmelanotide, as well as harm our competitive business position and our business prospects.

We also have licensed from Camurus its drug delivery technology, FluidCrystal, to formulate setmelanotide. Our license with Camurus imposes various obligations on us, and provides Camurus the right to terminate the license in the event of our material breach of the license agreement. Termination of our license from Camurus would result in our inability to use the licensed intellectual property.

We may enter into additional licenses to third-party intellectual property that are necessary or useful to our business. Future licensors may also allege that we have breached our license agreement and may accordingly seek to terminate our license with them. In addition, future licensors may have the right to terminate our license at will. Any termination could result in our loss of the right to use the licensed intellectual property, which could materially adversely affect our ability to develop and commercialize setmelanotide, if approved, as well as harm our competitive business position and our business prospects.

We have not yet registered trademarks for a commercial trade name for setmelanotide and failure to secure such registrations could adversely affect our business.

We have not yet registered trademarks for a commercial trade name for setmelanotide. Any future trademark applications may be rejected during trademark registration proceedings. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome them. In addition, in the U.S. PTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive those proceedings. Moreover, any name we propose to use for setmelanotide in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed product names, we may be required to expend significant additional resources in an effort to identify a suitable

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substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

If we do not obtain additional protection under the Hatch-Waxman Amendments and similar foreign legislation by extending the patent terms and obtaining product exclusivity for setmelanotide, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval for setmelanotide, one or more of the U.S. patents we license may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent term restoration of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, we may not be granted an extension because of, for example, failure to apply within applicable deadlines, failure to apply prior to expiration of relevant patents or otherwise failure to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our ability to generate revenues could be materially adversely affected.

While we believe that setmelanotide contains active ingredients that would be treated by the FDA as a new chemical entity, or a new drug product, and, therefore, if approved, should be afforded five years of marketing exclusivity, the FDA may disagree with that conclusion and may approve generic products within a period that is less than five years. Manufacturers may seek to launch these generic products following the expiration of the applicable marketing exclusivity period, even if we still have patent protection for setmelanotide. Competition that setmelanotide may face from generic versions could materially and adversely impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made in setmelanotide.

If we fail to obtain an extension of patent protection under similar foreign legislation, where applicable, our competitors may obtain approval of competing products following our patent expiration, and our ability to generate revenues could be materially adversely affected in the foreign countries concerned.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our product.

The United States has enacted and is currently implementing the America Invents Act of 2011, wide-ranging patent reform legislation. Further, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain future patents, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts and the U.S. PTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents or future patents.

We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

Our employees have been previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of the former employers of our employees. Litigation may be necessary to defend against these claims. Even if we

are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. If we fail in defending such claims, in addition to paying money damages, we may lose valuable intellectual property rights or personnel. A loss of key personnel or their work product could hamper or prevent our ability to commercialize setmelanotide, which would materially adversely affect our commercial development efforts.

Risks Related to Regulatory Approval and Marketing of Setmelanotide and Other Legal Compliance Matters

Even if we complete the necessary clinical trials, the regulatory and marketing approval process is expensive, time consuming and uncertain and may prevent us from obtaining approvals for the commercialization of setmelanotide. We depend entirely on the success of setmelanotide, which is in Phase 3 clinical development for treatment of POMC deficiency obesity and LepR deficiency obesity. We cannot be certain that we will be able to obtain regulatory approval for, or successfully commercialize, setmelanotide. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize setmelanotide, and our ability to generate revenue will be materially impaired.

We currently have only one product candidate, setmelanotide, in clinical development, and our business depends entirely on its successful clinical development, regulatory approval and commercialization. We currently have no drug products for sale and may never be able to develop marketable drug products. Setmelanotide, which is currently in Phase 3 clinical development as a treatment for genetic deficiencies affecting the MC4 pathway, including POMC deficiency obesity and LepR deficiency obesity, will require substantial additional clinical development, testing and regulatory approval before we are permitted to commence commercialization. The clinical trials of setmelanotide are, and the manufacturing and marketing of setmelanotide will be, subject to extensive and rigorous review and regulation by numerous government authorities in the United States and in other countries where we intend to test and, if approved, market setmelanotide. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through non-clinical testing and clinical trials that the product candidate is safe and effective for use in each target indication. This process can take many years and approval, if any, may be conditional on post-marketing studies and surveillance, and will require the expenditure of substantial resources beyond the proceeds we raise in this offering. When a sponsor relies exclusively or predominantly on foreign clinical data, the FDA may require a showing that those data are applicable to the U.S. population and U.S. medical practice, which in some cases may require bridging studies or other evidence. Of the large number of drugs in development in the United States and in other countries, only a small percentage will successfully complete the FDA regulatory approval process or the equivalent process in foreign jurisdictions and will be commercialized. In addition, we have not discussed all of our proposed development programs with the FDA or the competent authorities of foreign jurisdictions. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development and clinical trials, we cannot assure you that setmelanotide will be successfully developed or commercialized.

We are not permitted to market setmelanotide in the United States until we receive approval of an NDA from the FDA, or in any foreign jurisdictions until we receive the requisite approval from such countries. We have two Phase 3 clinical trials underway, one each for the treatment of POMC deficiency obesity and LepR deficiency obesity. Under our current development program, we plan to conduct a single Phase 3 clinical trial for POMC deficiency obesity. To date, in our ongoing discussions with the FDA, the agency has not asked for additional Phase 3 trials in POMC deficiency obesity, but the agency could still require us to conduct additional Phase 3 clinical trials for this indication. Moreover, for POMC deficiency obesity, the FDA could alter its previous advice on many aspects of the trial—the small size, the open label design, the amount of past medical history available on individual patients, the statistical analysis plan, the definition of clinically-relevant success for the protocol, entry of patients ages 12 or over—all of which may impact the timing and ability to obtain FDA approval. There are other aspects of the trial for which we

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have not received advice from the FDA, such as the number of U.S. versus non-U.S. patients and the number of patients with POMC gene defects versus the number of patients with PCSK1 defects, which could also impact the timing of and our ability to obtain FDA approval. We have not discussed the protocol for a Phase 3 program for LepR deficiency obesity with the FDA and thus we do not know if the FDA will provide advice on this trial that differs from the advice provided by the FDA for the trial in POMC deficiency obesity. Therefore, the timeline for enrollment, availability of data, and cost of conducting such trials are uncertain, and could be less favorable than those applicable to the POMC deficiency obesity program.

In addition, the FDA and other equivalent competent authorities in foreign jurisdictions will expect for there to be no introduction of bias in the open-label Phase 3 trials. Accordingly, we proposed to the FDA that little, if any, efficacy data will be available to us in any form until the Phase 3 trials are complete.

The FDA or other regulatory authorities and other equivalent competent authorities in foreign jurisdictions will also require that we conduct one or more pivotal trials for each other indication sought. In addition, we are not sure if one or more Phase 3 trials would be required for approval in each other indication. The need and length of placebo-controlled data in these pivotal trials and the number of patients required for these approvals is also unclear. We expect to seek an indication for obesity caused by monogenic deficiencies affecting the MC4 pathway. We are currently conducting Phase 3 trials for treatment of setmelanotide in POMC deficiency obesity and LepR deficiency obesity and Phase 2 trials for treatment of Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders. If the clinical data meet key primary and secondary endpoints for safety and efficacy, our overall clinical program may be less time consuming and require fewer patients than might a program for a broader obesity indication.

In the European Union we are currently conducting the Phase 3 clinical trial RM-493-012 in Germany and the United Kingdom. In France, the clinical trial application has recently been approved by the competent authorities. On March 23, 2017, we received EMA scientific advice on the appropriateness and sufficiency of the non-clinical and clinical development programs to support an initial marketing authorization application in POMC deficiency obesity. The EMA scientific advice included preliminary advice on the clinical trial RM-493-012. The EMA expressed general support for the ongoing Phase 3 program in POMC deficiency obesity. The EMA, advised that the regulatory strategy for a rare disorder is supported, and that the EMA may have to rely on scarce data. The EMA advised, however, that we need to consider whether full approval, approval under conditional or exceptional circumstances would be the most appropriate pathway for application for POMC deficiency obesity.

Given the orphan status of setmelanotide for the treatment of POMC deficiency in the European Union the marketing authorization application for a POMC deficiency obesity indication will be submitted via the centralized procedure. In addition, we plan to submit a pediatric investigation plan for setmelanotide to the EMA Pediatric Development Committee in 2017.

We cannot assure you that the clinical trials we are conducting in the European Union will be completed within this timeline. Similar to the United States, we are subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual EU member states where we are conducting our clinical trials. Failure by us or by any of our third party partners to comply with EU laws and the related national laws of individual EU member states governing the conduct of clinical trials may result in the suspension of clinical trials and in other administrative, civil, or criminal penalties.

Our plan is to expand our internal clinical development operations and capabilities so that we can continue to enroll and manage our Phase 2 clinical trials, and enroll and manage our Phase 3 clinical trials, such that, if the clinical trials are successful, we can file an NDA for POMC deficiency obesity in the United States by 2019. We believe we have finalized the design, timing and size of our Phase 3 trial for POMC deficiency obesity with the FDA but we cannot assure you that the trial will not be subject to further modification or that it will be completed on time. In addition, obtaining approval of an NDA and

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the approval of a marketing authorization application from the European Commission is a complex, lengthy, expensive and uncertain process, and the FDA, EMA or equivalent competent authorities in foreign jurisdictions may delay, limit or deny approval of setmelanotide for many reasons, including, among others:

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may disagree with our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials;
- we may not be able to demonstrate to the satisfaction of the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions that setmelanotide is safe and effective in treating obesity caused by certain genetic deficiencies affecting the MC4 pathway;
- the results of our clinical trials may not be interpretable or meet the level of statistical or clinical significance required by the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions for marketing approval. For example, the potential unblinding of setmelanotide studies due to easily identifiable adverse events may raise the concern that potential bias has affected the clinical trial results;
- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may disagree with the number, size, conduct or implementation of our clinical trials;
- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may require that we conduct additional clinical trials or pre-clinical studies;
- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions or the applicable foreign regulatory agency may identify deficiencies in our chemistry, manufacturing or controls of setmelanotide;
- the CROs that we retain to conduct our clinical trials may take actions outside of our control that materially adversely impact our clinical trials;
- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may find the data from preclinical studies and clinical trials insufficient to demonstrate that clinical and other benefits of setmelanotide outweigh its safety risks;
- the FDA, the EMA, or other equivalent competent authorities in foreign may disagree with our interpretation of data from our preclinical studies and clinical trials;
- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may not approve the formulation, labeling or specifications of setmelanotide;
- the FDA, the EMA, or other equivalent competent authorities in foreign may not accept data generated at our clinical trial sites;
- if and when our NDA or our marketing authorization application is submitted and reviewed by an advisory committee, the FDA, the EMA, or the equivalent competent authorities in foreign jurisdictions may have difficulties scheduling an advisory committee meeting in a timely manner or the advisory committee may recommend against approval of our application or may recommend that the FDA, the EMA, or the equivalent competent authorities in foreign jurisdictions require, as a condition of approval, additional preclinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;
- the FDA may require development of a REMS as a condition of approval or post-approval, or may not agree with our proposed REMS or may impose additional requirements that limit the promotion, advertising, distribution, or sales of setmelanotide. In addition, the European Commission may grant only conditional approval marketing authorization or impose specific obligations as a condition for marketing authorization, or may require us to conduct post authorization safety studies as a condition of grant of marketing authorization;

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- the FDA or other equivalent competent foreign regulatory agency may deem our manufacturing processes or our facilities or the facilities of our CMOs inadequate to preserve the identity, strength, quality, purity, or potency of our product; or
- the FDA, the European Commission, or the equivalent competent authorities in foreign jurisdictions may change its approval policies or adopt new regulations and guidance.

Any of these factors, many of which are beyond our control, could jeopardize our ability to obtain regulatory approval for and successfully market setmelanotide. Moreover, because our business is entirely dependent upon setmelanotide, any such setback in our pursuit of regulatory approval would have a material adverse effect on our business and prospects.

Our failure to obtain marketing approval in foreign jurisdictions would prevent setmelanotide from being marketed abroad, and any approval we are granted for setmelanotide in the United States would not assure approval of setmelanotide in foreign jurisdictions.

In order to market and sell setmelanotide and any other product candidate that we may develop in the European Union and many other jurisdictions, we or our third-party collaborators must obtain separate marketing authorizations and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be sold in that country. We or these third parties may not obtain approvals from competent authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by competent authorities in other countries or jurisdictions, and approval by one competent authority outside the United States does not ensure approval by competent authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize setmelanotide in any market. Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of setmelanotide in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing setmelanotide in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for setmelanotide, which could significantly and materially harm our business.

Even if we obtain marketing approval for setmelanotide, the terms of approval and ongoing regulation may limit how we manufacture and market setmelanotide and compliance with such requirements may involve substantial resources, which could materially impair our ability to generate revenue.

Even if we receive marketing approval for setmelanotide, regulatory authorities may impose significant restrictions on setmelanotide's indicated uses or marketing or impose ongoing requirements for potentially costly post approval studies. Setmelanotide will also be subject to ongoing requirements by the FDA, the EMA, and the competent authorities in the EU member states, governing labeling, packaging, storage advertising, promotion, marketing, distribution, importation, exportation, post-approval, manufacturing, recordkeeping, and submission of safety and other post market information. The FDA and the other competent foreign authorities have significant post market authority, including, for example, the authority to require labeling changes based on new safety information and to require post market studies

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or clinical trials to evaluate serious safety risks related to the use of a drug. The FDA also has the authority to require, as part of an NDA or post approval, the submission of a REMS, which may include Elements to Assure Safe Use, or ETASU. Any REMS required by the FDA may lead to increased costs to assure compliance with new post approval regulatory requirements and potential requirements or restrictions on the sale of approved products, all of which could lead to lower sales volume and revenue.

Manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other equivalent competent authorities for compliance with cGMPs and other regulations. If we or a regulatory agency discover problems with setmelanotide, such as adverse events of unanticipated severity or frequency, or problems with the facility where setmelanotide is manufactured, a regulatory agency may impose restrictions on setmelanotide, the manufacturer or us, including requiring withdrawal of setmelanotide from the market or suspension of manufacturing. If we, setmelanotide or the manufacturing facilities for setmelanotide fail to comply with applicable regulatory requirements, a regulatory agency may, among other things:

- issue warning letters or untitled letters;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw marketing approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications submitted by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain setmelanotide, refuse to permit the import or export of setmelanotide, or request that we initiate a product recall.

Accordingly, assuming we receive marketing approval for setmelanotide, we and our CMOs will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we are not able to comply with post-approval regulatory requirements, we could have the marketing approvals for setmelanotide withdrawn by regulatory authorities and our ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Thus, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Similar to the United States, both marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual EU member states, both before and after grant of the manufacturing and Marketing Authorizations. This oversight includes control of compliance with cGMP rules, which govern quality control of the manufacturing process and require documentation policies and procedures. We and our third party manufacturers would be required to ensure that all of our processes, methods, and equipment are compliant with cGMP. Failure by us or by any of our third party partners, including suppliers, manufacturers, and distributors to comply with EU laws and the related national laws of individual EU member states governing the conduct of clinical trials, manufacturing approval, marketing authorization of medicinal products, both before and after grant of marketing authorization, and marketing of such products following grant of authorization may result in administrative, civil, or criminal penalties. These penalties could include delays in or refusal to authorize the conduct of clinical trials or to grant Marketing Authorization, product withdrawals and recalls, product seizures, suspension, or variation of the marketing authorization, total or partial suspension of production, distribution, manufacturing, or clinical trials, operating restrictions, injunctions, suspension of licenses, fines, and criminal penalties.

In addition, EU legislation related to pharmacovigilance, or the assessment and monitoring of the safety of medicinal products, provides that the EMA and the competent authorities of the EU member states have the authority to require companies to conduct additional post-approval clinical efficacy and

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safety studies. The legislation also governs the obligations of marketing authorization holders with respect to additional monitoring, adverse event management and reporting. Under the pharmacovigilance legislation and its related regulations and guidelines, we may be required to conduct a labor intensive collection of data regarding the risks and benefits of marketed products and may be required to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical studies, which may be time-consuming and expensive and could impact our profitability. Non-compliance with such obligations can lead to the variation, suspension or withdrawal of marketing authorization or imposition of financial penalties or other enforcement measures.

Recently enacted and future healthcare reform legislation or regulation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize setmelanotide and may adversely affect the prices we, or they, may obtain and may have a negative impact on our business and results of operations.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of setmelanotide, restrict or regulate post-approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any products for which we, or they, obtain marketing approval. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for any approved products.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA. Among the provisions of the ACA of importance to our business, including, without limitation, our ability to commercialize and the prices we may obtain for any of setmelanotide and that are approved for sale, are the following:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee does not apply to sales of certain products approved exclusively for orphan indications;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expansion of manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;
- introduction of a price reporting requirement for drugs that are inhaled, instilled, implanted, injected, or infused and not generally dispensed through retail community pharmacies;
- addition of more entity types eligible for participation in the Public Health Service the 340B drug pricing program, or the 340B program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;

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- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. However, the IPAB implementation has been not been clearly defined. ACA provided that under certain circumstances, IPAB recommendations or recommendations of the Secretary of Health and Human Services will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. For example, beginning April 1, 2013, Medicare payments for all items and services, including drugs and biologics, were reduced by 2% under the sequestration (i.e., automatic spending reductions) required by the Budget Control Act of 2011, as amended by the American Taxpayer Relief Act of 2012. Subsequent legislation extended the 2% reduction, on average, to 2025. Sequestration may result in additional reductions in Medicare and other healthcare funding and, if we obtain regulatory approvals, may otherwise affect the prices we may obtain for setmelanotide or the frequency with which setmelanotide is prescribed or used if approved.

Legislative changes to or regulatory changes under the ACA remain possible and appear likely in the 115th U.S. Congress and under the Trump administration. The nature and extent of any legislative or regulatory changes to the ACA, including repeal and replacement initiatives, are uncertain at this time. It is possible that ACA repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. The scope of potential future legislation to modify or repeal and replace ACA provisions is highly uncertain in many respects.

Additional changes that may affect our business include the expansion of new programs such as Medicare payment for performance initiatives for physicians under the Medicare Access and CHIP Reauthorization Act of 2015, or MACRA, which will be fully implemented in 2019. At this time, it is unclear how the introduction of the Medicare quality payment program will impact overall physician reimbursement. The costs of prescription pharmaceuticals in the United States has also been the subject of considerable discussion in the United States, and members of Congress and the Administration have stated that they will address such costs through new legislative and administrative measures. This focus has resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products.

We expect that these and other healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved drug. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drugs. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our drug candidates or additional pricing pressures.

The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some

countries, we may be required to conduct a clinical trial that compares the cost effectiveness of setmelanotide to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.

If we participate in the Medicaid Drug Rebate Program and fail to comply with our reporting and payment obligations under that program or other governmental pricing programs that we participate in, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We expect to participate in and have certain price reporting obligations to the Medicaid Drug Rebate program. Under the Medicaid Drug Rebate program, if we successfully commercialize setmelanotide, we would be required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being made available to the states for our drugs under Medicaid and Medicare Part B. Those rebates are based on pricing data we would have to report on a monthly and quarterly basis to the Centers for Medicare and Medicaid Services, or CMS, the federal agency that administers the Medicaid Drug Rebate program. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug which, in general, represents the lowest price available from the manufacturer to any entity in the U.S. in any pricing structure, calculated to include all sales and associated rebates, discounts and other price concessions. Our failure to comply with these price reporting and rebate payment obligations if we participate in the program could negatively impact our financial results.

Federal law requires that any company that participates in the Medicaid Drug Rebate program also participate in the 340B program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B program requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The ACA expanded the list of covered entities to include certain free-standing cancer hospitals, critical access hospitals, rural referral centers and sole community hospitals, but exempts "orphan drugs" from the ceiling price requirements for these covered entities. The 340B ceiling price is calculated using a statutory formula based on the average manufacturer price and rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate program, and in general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. Any additional future changes to the definition of average manufacturer price and the Medicaid rebate amount under the ACA or other legislation or regulation could affect our 340B ceiling price calculations and negatively impact our results of operations if we successfully commercialize setmelanotide. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in an inpatient setting.

In order to be eligible to have our products that we successfully commercialize paid for with federal funds under the Medicaid program and purchased by certain federal agencies and grantees, we also would have to participate in the U.S. Department of Veterans Affairs, or VA, Federal Supply Schedule, or FSS, pricing program. As part of this program, we would be obligated to make our products available for procurement on an FSS contract under which we must comply with standard government terms and conditions and charge a price that is no higher than the statutory Federal Ceiling Price, or FCP, to four federal agencies (VA, U.S. Department of Defense, or DOD, Public Health Service, and U.S. Coast Guard).

Civil monetary penalties can be applied if we participate in these programs and if we are found to have knowingly submitted any false price information to the government or if we fail to submit the required price data on a timely basis. Such conduct also could be grounds for CMS to terminate the Medicaid drug rebate agreement pursuant to which we would participate in the Medicaid drug rebate program, in which case federal payments may not be available under Medicaid for our covered outpatient drugs. We cannot assure you that our submissions will not be found by CMS or another government agency to be incomplete or incorrect.

If we obtain marketing approval for setmelanotide, we will be subject to strict enforcement of post-marketing requirements and we could be subject to substantial penalties, including withdrawal of our product from the market, if we fail to comply with all regulatory requirements.

If we obtain marketing approval for setmelanotide, we will be subject to continual requirements of and review by the FDA and equivalent competent authorities in foreign jurisdictions. These requirements may include, but are not limited to, post-approval studies to be conducted which may include carcinogenicity studies, a QT interval prolongation study in one form or another, and ongoing natural history studies with patient registries. Other requirements may also include, among other things, restrictions governing promotion of an approved product, submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. The FDA and other federal and state agencies, including the Department of Justice and other equivalent competent authorities in foreign jurisdictions, closely regulate compliance with all requirements governing prescription drug products, including requirements pertaining to marketing and promotion of drugs in accordance with the provisions of the approved labeling and manufacturing of products in accordance with cGMP requirements. Violations of such requirements may lead to investigations alleging violations of the FDCA, and other statutes, including the False Claims Act and other federal and state health care fraud and abuse laws as well as state consumer protection laws.

For example, the FDA and other equivalent competent authorities in foreign jurisdictions strictly regulate the promotional claims that may be made about prescription products, such as setmelanotide, if approved. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. If we receive marketing approval for setmelanotide as a treatment for obesity caused by certain genetic deficiencies affecting the MC4 pathway, physicians may nevertheless prescribe setmelanotide to their patients in a manner that is inconsistent with the approved labeling. If we are found to have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. Oversight and management of promotional practices may require operational changes and additions, if setmelanotide is approved and commercialized. If we cannot successfully manage the promotion of setmelanotide, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

In the European Union, the advertising and promotion of our products are subject to EU laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual EU member states may apply to the advertising and promotion of medicinal products. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities. The SmPC is the document that provides information to physicians concerning the safe and effective use of the medicinal product. It forms an intrinsic and integral part of the marketing authorization granted for the medicinal

product. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion. The off-label promotion of medicinal products is prohibited in the European Union. The applicable laws at European Union level and in the individual EU member states also prohibit the direct-to-consumer advertising of prescription-only medicinal products. Violations of the rules governing the promotion of medicinal products in the European Union could be penalized by administrative measures, fines and imprisonment. These laws may further limit or restrict the advertising and promotion of our products to the general public and may also impose limitations on our promotional activities with health care professionals.

We may be subject to federal and state healthcare laws and regulations. If we are unable to comply or have not fully complied with such laws and regulations, we could face criminal sanctions, damages, civil penalties, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and others will play a primary role in the recommendation and prescription of setmelanotide, if approved. Our arrangements and interactions with healthcare professionals, third-party payors, patients and others will expose us to broadly applicable fraud and abuse, anti-kickback, false claims and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute setmelanotide, if we obtain marketing approval. The U.S. federal and state healthcare laws and regulations that may affect our ability to operate include, but are not limited to:

- The United States federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, or receiving remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease order or arranging for or recommending of the purchase, lease or order of any good or service for which payment may be made, in whole or in part, by federal healthcare programs such as Medicare and Medicaid. This statute has been interpreted to apply to arrangements between pharmaceutical companies on one hand and prescribers, purchasers and formulary managers on the other. Liability under the Anti-Kickback Statute may be established without proving actual knowledge of the statute or specific intent to violate it. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. Although there are a number of statutory exemptions and regulatory safe harbors to the federal Anti-Kickback Statute protecting certain common business arrangements and activities from prosecution or regulatory sanctions, the exemptions and safe harbors are drawn narrowly. Practices that involve remuneration to those who prescribe, purchase, or recommend pharmaceutical and biological products, including certain discounts, or engaging such individuals as consultants, advisors, or speakers, may be subject to scrutiny if they do not fit squarely within an exemption or safe harbor. Our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability. Moreover, there are no safe harbors for many common practices, such as educational and research grants, charitable donations, product support and patient assistance programs.
- The federal civil False Claims Act prohibits individuals or entities from, among other things, knowingly presenting, or causing to be presented a false or fraudulent claim for payment of government funds, or knowingly making, using or causing to made or used a false record or statement material to an obligation to pay money to the government or knowingly concealing or knowingly and improperly avoiding, decreasing or concealing an obligation to pay money to the federal government. Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Many pharmaceutical manufacturers have been investigated and have reached substantial financial settlements with the federal government under the civil False Claims Act for a variety of alleged improper activities including causing false claims to be submitted as a result of the marketing of their products for

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unapproved and thus non-reimbursable uses, inflating prices reported to private price publication services which are used to set drug payment rates under government healthcare programs, and other interactions with prescribers and other customers including those that may have affected their billing or coding practices and submission to the federal government. The government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. Pharmaceutical and other healthcare companies also are subject to other federal false claims laws, including, among others, federal criminal healthcare fraud and false statement statutes that extend to non-government health benefit programs.

- The federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.
- HIPAA and the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statement or entry in connection with the delivery of or payment for healthcare benefits, items or services.
- Numerous federal and state laws and regulations that address privacy and data security, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the FTC Act), govern the collection, use, disclosure and protection of health-related and other personal information.
- The federal transparency requirement known as the federal Physician Payments Sunshine Act, being implemented as the Open Payments Program, requires certain manufacturers of drugs, devices, biologics and medical supplies to report payments and other transfers of value to physicians and teaching hospitals, as well as ownership and investments interests held by physicians and their immediate family members. Pharmaceutical and biological manufacturers with products for which payment is available under Medicare, Medicaid or the State Children's Health Insurance Program are required to submit a report to the Centers for Medicare and Medicaid Services within the U.S. Department of Health and Human Services on or before the 90th day of each calendar year disclosing reportable payments made in the previous calendar year.
- Analogous state laws and regulations, such as state anti-kickback and false claims laws, which may apply to items or services reimbursed under Medicaid and other state programs or, in several states, regardless of the payer. Some state laws also require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products and to report gifts and payments to certain health care providers in those states. Some of these states also prohibit certain marketing-related activities including the provision of gifts, meals, or other items to certain health care providers. In addition, California, Connecticut, Nevada, and Massachusetts require pharmaceutical companies to implement compliance programs or marketing codes of conduct.

Ensuring that our business arrangements and interactions with healthcare professionals, third-party payors, patients and others comply with applicable healthcare laws and regulations will require substantial resources. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including anticipated activities to be conducted by our sales and marketing team, were found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines and exclusion from government funded healthcare programs, such as Medicare.

and Medicaid, the curtailment or restructuring of our operation, any of which could substantially disrupt our operations. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws or regulations, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business.

Our employees may engage in misconduct or other improper activities, including violating applicable regulatory standards and requirements or engaging in insider trading, which could significantly harm our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with the regulations of the FDA and applicable non-U.S. regulators, provide accurate information to the FDA and applicable non-U.S. regulators, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of, including trading on, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and any precautions we take to detect and prevent this activity may be ineffective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Our failure to comply with data protection laws and regulations could lead to government enforcement actions and significant penalties against us, and adversely impact our operating results.

We are subject to U.S. data protection laws and regulations (i.e., laws and regulations that address privacy and data security) at both the federal and state levels. The legislative and regulatory landscape for data protection continues to evolve, and in recent years there has been an increasing focus on privacy and data security issues. Numerous federal and state laws, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the FTC Act), govern the collection, use, and disclosure and protection of health-related and other personal information. Failure to comply with data protection laws and regulations could result in government enforcement actions and create liability for us, which could include civil and/or criminal penalties, private litigation and/or adverse publicity that could negatively affect our operating results and business. In addition, we may obtain health information from third parties, such as research institutions with which we collaborate, that are subject to privacy and security requirements under HIPAA. Although we are not directly subject to HIPAA, other than potentially with respect to providing certain employee benefits, we could be subject to criminal penalties if we knowingly obtain or disclose individually identifiable health information maintained by a HIPAA covered entity in a manner that is not authorized or permitted by HIPAA.

EU member states, Switzerland and other countries have also adopted data protection laws and regulations, which impose significant compliance obligations. In the European Union, the collection and use of personal health data is governed by the provisions of the EU Data Protection Directive. The European Union Data Protection Directive and the national implementing legislation of the EU member states impose strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. In particular, these obligations and restrictions concern the consent of the individuals to whom the personal data relates, the information

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provided to the individuals, notification of data processing obligations to the competent national data protection authorities and the security and confidentiality of the personal data. Data protection authorities from the different EU member states may interpret the EU Data Protection Directive and national laws differently and impose additional requirements, which add to the complexity of processing personal data in the European Union.

Guidance on implementation and compliance practices are often updated or otherwise revised. For example, the EU Data Protection Directive prohibits the transfer of personal data to countries outside of the European Union, including the United States, that are not considered by the European Commission to provide an adequate level of data protection.

The judgment by the Court of Justice of the European Union in Case C-362/14 Maximillian Schrems v. Data Protection Commissioner, or the Schrems case, held that the Safe Harbor Framework, which was relied upon by many United States entities as a basis for transfer of personal data from the European Union to the United States, was invalid. United States entities therefore, had only the possibility to rely on the alternate procedures for such data transfer provided in the EU Data Protection Directive.

On February 29, 2016, however, the European Commission announced an agreement with the United States Department of Commerce, or the DOC, to replace the invalidated Safe Harbor framework with a new "Privacy Shield". On July 12, 2016, the European Commission adopted a decision on the adequacy of the protection provided by the Privacy Shield. The Privacy Shield is intended to address the requirements set out by the Court of Justice of the European Union in the Schrems case. The Privacy Shield imposes more stringent obligations on companies, provides stronger monitoring and enforcement by the DOC and the Federal Trade Commission, and makes commitments on the part of public authorities regarding access to information. United States entities have been able to certify to the DOC their compliance with the privacy principles of the Privacy Shield since August 1, 2016 and rely on the Privacy Shield certification to transfer of personal data from the European Union to the United States.

In September 2016, the Irish privacy advocacy group Digital Rights Ireland brought an action for annulment of the European Commission decision on the adequacy of the Privacy Shield before the Court of Justice of the EU, Case T-670/16. In October 2016, a further action for annulment was brought by three French digital rights advocacy group, La Quadrature du Net, French Data Network and the Fédération FDN, Case T-738/16. Both cases are currently pending before the European Court of Justice. If the Court of Justice of the European Union invalidates the Privacy Shield, it will no longer be possible to rely on the Privacy Shield certification to transfer personal data from the European Union to entities in the United States. Adherence to the Privacy Shield is not, however, mandatory. Entities based in the United States are permitted to rely either on their adherence to the Privacy Shield or on the other authorized means and procedures to transfer personal data provided by the EU Data Protection Directive.

In addition, the EU Data Protection Regulation entered into force on May 24, 2016 and will apply from May 25, 2018. The EU Data Protection Regulation will introduce new data protection requirements in the European Union and substantial fines for breaches of the data protection rules. The EU Data Protection Regulation will increase our responsibility and liability in relation to personal data that we process, and we may be required to put in place additional mechanisms to ensure compliance with the new data protection rules.

Our failure to comply with these laws, or changes in the way in which these laws are implemented, could lead to government enforcement actions and significant penalties against us, and adversely impact our operating results.

Our future growth depends, in part, on our ability to penetrate foreign markets, where we will be subject to additional regulatory burdens and other risks and uncertainties.

Our future profitability will depend, in part, on our ability to commercialize setmelanotide in foreign markets for which we intend to rely on collaborations with third parties. If we commercialize setmelanotide in foreign markets, we will be subject to additional risks and uncertainties, including:

- our customers' ability to obtain reimbursement for setmelanotide in foreign markets;
- our inability to directly control commercial activities because we are relying on third parties;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- longer lead times for shipping;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries;
- foreign currency exchange rate fluctuations; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Foreign sales of setmelanotide could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling setmelanotide outside of the United States and require us to develop and implement costly compliance programs.

If we expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act of 1977, or the FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of such third party in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the company, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security

purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing or selling certain product candidates and products outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The Securities and Exchange Commission, or SEC, also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

The results of the United Kingdom's referendum on withdrawal from the European Union may have a negative effect on global economic conditions, financial markets and our business.

On March 29, 2017, the Government of the United Kingdom initiated the formal procedure of withdrawal from the European Union. The procedure involves a two-year negotiation period in which the United Kingdom and the European Union must conclude an agreement setting out the terms of the United Kingdom's withdrawal and the arrangements for the United Kingdom's future relationship with the European Union. This negotiation period could be extended by a unanimous decision of the European Council, in agreement with the United Kingdom.

The referendum has created significant uncertainty concerning the future relationship between the United Kingdom and the European Union. This includes the laws and regulations that will apply as the United Kingdom determines which European Union laws to replace or replicate in the event of a withdrawal. From a regulatory perspective, the United Kingdom's withdrawal could result in significant complexity and risks. A basic requirement related to the grant of a marketing authorization for a medicinal product in the European Union is the requirement that the applicant is established in the European Union. Following withdrawal of the United Kingdom from the European Union, marketing authorizations previously granted to applicants established in the United Kingdom may no longer be valid. Moreover, depending upon the exact terms of the United Kingdom's withdrawal, there is an arguable risk that the scope of a marketing authorization for a medicinal product granted by the European Commission pursuant to the centralized procedure would not, in the future, include the United Kingdom. In these circumstances, an authorization granted by the United Kingdom's competent authorities would always be required to place medicinal products on the United Kingdom market.

In addition, the laws and regulations that will apply after the United Kingdom withdraws from the European Union may have implications for manufacturing sites that hold certification issued by the United Kingdom competent authorities. Our capability to rely on these manufacturing sites for products intended for the European Union market would also depend upon the exact terms of the United Kingdom's withdrawal.

The United Kingdom referendum has also given rise to calls for the governments of other EU member states to consider withdrawal from the European Union. These developments, or the perception that they could occur, have had and may continue to have a material adverse effect on global economic conditions and the stability of global financial markets. They may significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets.

The efforts of the Trump administration to pursue regulatory reform may limit the FDA's ability to engage in oversight and implementation activities in the normal course, and that could negatively impact our business.

The Trump administration has taken several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. On January 30, 2017, President

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Trump issued an executive order, applicable to all executive agencies, including the FDA, that requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This executive order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the executive order requires agencies to identify regulations to offset any incremental cost of a new regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within the Office of Management and Budget, or OMB, on February 2, 2017, the administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain our key employees and consultants, and to attract, retain and motivate qualified personnel.

We are highly dependent on Keith M. Gottesdiener, M.D., our Chief Executive Officer and President, Hunter Smith, our Chief Financial Officer and Treasurer, Nithya Desikan, our Chief Commercial Officer, Lex H.T. Van der Ploeg, Ph.D., our Chief Scientific Officer, and Fred T. Fidorek, M.D., our Chief Medical Officer. We have employment agreements with these individuals and have entered into new employment agreements with each of them which will become effective upon consummation of this offering, but any individual may terminate his or her employment with us at any time. The loss of their services might impede the achievement of our research, development and commercialization objectives. We also do not have any key-person life insurance on any of these key employees. We rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us and may not be subject to non-compete agreements. Recruiting and retaining qualified scientific personnel and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel.

We will need to develop and expand our company, and we may encounter difficulties in managing this development and expansion, which could disrupt our operations.

In connection with becoming a public company, we expect to increase our number of employees and the scope of our operations. In particular, we will need to transition from a research and development company to a commercial company. To manage our anticipated development and expansion, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Also, our management may need to divert a disproportionate amount of its attention away from their day-to-day activities and devote a substantial amount of time to managing these development activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, and give rise to operational mistakes, loss of business and commercial opportunities, loss of employees and reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs and

may divert financial resources from other projects, such as the development of setmelanotide. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize setmelanotide, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our company.

In order to satisfy our obligations as a public company, we will need to hire additional qualified accounting and financial personnel with appropriate public company experience.

As a newly public company, we will need to establish and maintain effective disclosure and financial controls and make changes in our corporate governance practices. We will need to hire additional accounting and financial personnel with appropriate public company experience and technical accounting knowledge, and it may be difficult to recruit and retain such personnel. Even if we are able to hire appropriate personnel, our existing operating expenses and operations will be impacted by the direct costs of their employment and the indirect consequences related to the diversion of management resources from product development efforts.

Our internal computer systems, or those of our third-party CROs, CMOs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of setmelanotide development programs.

Our internal computer systems and those of our third-party CROs, CMOs, and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of clinical trial data for setmelanotide could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidate, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of setmelanotide could be delayed.

We may acquire businesses or products, form strategic alliances or create joint ventures in the future, and we may not realize their benefits.

We may acquire additional businesses or products, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new products resulting from a strategic alliance, joint venture or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition, we will achieve the expected synergies to justify the transaction.

Risks Related to Our Common Stock and This Offering

Our executive officers, directors, principal stockholders and their affiliates will continue to exercise significant control over our company after this offering, which will limit your ability to influence corporate matters and could delay or prevent a change in corporate control.

Upon the completion of this offering, the existing holdings of our executive officers, directors, principal stockholders and their affiliates, including Pfizer Inc., investment funds affiliated with MPM Bioventures V LLC, investment funds affiliated with TRV GP, LLC, investment funds affiliated with New Enterprise Associates 13, L.P. and NEA Ventures 2009, L.P., investment funds affiliated with two public

healthcare investment funds, investment funds affiliated with Deerfield Mgmt, L.P. and J.E. Flynn Capital III, LLC, Sutrepa SAS and investment funds affiliated with OrbiMed Advisors LLC will represent beneficial ownership, in the aggregate, of approximately 68% of our outstanding common stock, assuming no exercise of the underwriters' option to acquire additional common stock in this offering and assuming we issue the number of shares of common stock as set forth on the cover page of this prospectus not including any shares purchased by these stockholders in this offering. As a result, these stockholders, if they act together, will be able to influence our management and affairs and control the outcome of matters submitted to our stockholders for approval, including the election of directors and any sale, merger, consolidation or sale of all or substantially all of our assets. These stockholders acquired their shares of common stock for substantially less than the price of the shares of common stock being acquired in this offering, and these stockholders may have interests, with respect to their common stock, that are different from those of investors in this offering and the concentration of voting power among these stockholders may have an adverse effect on the price of our common stock. In addition, this concentration of ownership might adversely affect the market price of our common stock by:

- delaying, deferring or preventing a change of control of us;
- impeding a merger, consolidation, takeover or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

Certain of our existing principal stockholders, directors and their affiliated entities, have indicated an interest in purchasing an aggregate of approximately \$40.0 million in shares of our common stock in this offering at the initial public offering price per share and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers, and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering. The foregoing discussion does not reflect any potential purchases by these potential purchasers.

See "Principal Stockholders" for more information regarding the ownership of our outstanding common stock by our executive officers, directors, principal stockholders and their affiliates.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, even one that may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

We are a Delaware corporation. Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may delay or prevent an acquisition of us or a change in our management. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Although we believe these provisions collectively will provide for an opportunity to obtain greater value for stockholders by requiring potential acquirers to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management. Any provision in our amended and restated certificate of incorporation and amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.

You will suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase in this offering. Assuming an initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, purchasers of common stock in this offering will experience immediate dilution of \$10.08 per share in net tangible book value of the common stock. In addition, investors purchasing common stock in this offering will contribute 55% of the total amount invested by stockholders since inception but will only own 26% of the shares of common stock outstanding. See "Dilution" for a more detailed description of the dilution to new investors in the offering.

An active trading market for our common stock may not develop, and you may not be able to resell your shares at or above the initial public offering price.

Prior to this offering, there has been no public market for shares of our common stock. Although we anticipate our common stock will be approved for listing on the NASDAQ Global Market, an active trading market for our shares may never develop or be sustained following this offering. The initial public offering price of our common stock will be determined through negotiations between us and the underwriters. This initial public offering price may not be indicative of the market price of our common stock after this offering. In the absence of an active trading market for our common stock, investors may not be able to sell their common stock at or above the initial public offering price or at the time that they would like to sell.

If securities or industry analysts do not publish research or reports or publish unfavorable research or reports about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us, our business, our market or our competitors. We do not control these analysts. We do not currently have and may never obtain research coverage by securities and industry analysts. If no securities or industry analysts commence coverage of our company, the trading price for our stock would be negatively impacted. In the event we obtain securities or industry analyst coverage, if one or more of the analysts who covers us downgrades our stock, our stock price would likely decline. If one or more of these analysts issues unfavorable commentary or ceases to cover us or fails to regularly publish reports on us, interest in our stock could decrease, which could cause our stock price or trading volume to decline.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the global financial crisis, could result in a variety of risks to our business, including weakened demand for setmelanotide and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

Market volatility may affect our stock price and the value of your investment.

Following this offering, the market price for our common stock is likely to be volatile, in part because our common stock has not been previously traded publicly. In addition, the market price of our common

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stock may fluctuate significantly in response to a number of factors, most of which we cannot control, including, among others:

- plans for, progress of, or results from preclinical studies and clinical trials of setmelanotide;
- the failure of the FDA to approve setmelanotide;
- announcements of new products, technologies, commercial relationships, acquisitions or other events by us or our competitors;
- the success or failure of other weight loss therapies and companies targeting rare diseases and orphan drug treatment;
- regulatory or legal developments in the United States and other countries;
- failure of setmelanotide, if approved, to achieve commercial success;
- fluctuations in stock market prices and trading volumes of similar companies;
- general market conditions and overall fluctuations in U.S. equity markets;
- variations in our quarterly operating results;
- changes in our financial guidance or securities analysts' estimates of our financial performance;
- changes in accounting principles;
- our ability to raise additional capital and the terms on which we can raise it;
- sales of large blocks of our common stock, including sales by our executive officers, directors and significant stockholders;
- additions or departures of key personnel;
- discussion of us or our stock price by the press and by online investor communities; and
- other risks and uncertainties described in these risk factors.

Our quarterly operating results may fluctuate significantly.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expenses related to our development programs;
- addition or termination of clinical trials;
- any intellectual property infringement lawsuit in which we may become involved;
- regulatory developments affecting setmelanotide;
- our execution of any collaborative, licensing or similar arrangements, and the timing of payments we may make or receive under these arrangements;
- the achievement and timing of milestone payments under our existing collaboration and license agreements; and
- if setmelanotide receives regulatory approval, the level of underlying demand for that product and customers' buying patterns.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially.

We will have broad discretion in how we use the proceeds of this offering. We may not use these proceeds effectively, which could affect our results of operations and cause our stock price to decline.

We will have considerable discretion in the application of the net proceeds of this offering. We intend to use the net proceeds from this offering to fund development and manufacturing of setmelanotide through completion of our Phase 3 clinical trials and subsequent NDA submissions with the FDA for the treatment of POMC deficiency obesity and LepR deficiency obesity, the development of setmelanotide through our Phase 2 proof of concept clinical trials for Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity and POMC epigenetic disorders, as well as the initiation of our Phase 3 clinical trials for Bardet-Biedl syndrome, the preparation for commercialization of setmelanotide, initiatives to expand the diagnosis of genetic obesity, including research and scientific exchange related to our ongoing genotyping and genetic epidemiology studies and for working capital and general administrative expenses, additional research and development expenses, and other general corporate purposes. As a result, investors will be relying upon management's judgment with only limited information about our specific intentions for the use of the net proceeds of this offering. We may use the net proceeds for purposes that do not yield a significant return or any return at all for our stockholders. In addition, pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

Our ability to use certain net operating loss carryovers and other tax attributes may be limited.

We have incurred substantial losses during our history and we do not expect to become profitable in the near future and may never achieve profitability. Under the Internal Revenue Code of 1986, as amended, or the Code, a corporation is generally allowed a deduction for net operating losses, or NOLs, carried over from a prior taxable year. Under that provision, we can carry forward certain taxable losses of our subsidiaries to offset future taxable income, if any, until such losses are used or expire. The same is true of other unused tax attributes, such as research tax credits. As of December 31, 2016, we had approximately \$46.9 and \$24.4 million of unused federal and state carryforwards of NOLs, respectively, and approximately \$1.0 and \$0.4 million of unused federal and state carryforwards of tax credits, respectively.

If a corporation undergoes an "ownership change," generally defined as a greater than 50% change by value in its equity ownership over a three-year period, Sections 382 and 383 of the Code limit the corporation's ability to use carryovers of its pre-change NOLs, credits and certain other tax attributes to reduce its tax liability for periods after the ownership change. Our issuance of common stock pursuant to this offering may result in a limitation under Sections 382 and 383, either separately or in combination with certain prior or subsequent shifts in the ownership of our common stock. As a result, our ability to use carryovers of pre-change NOLs and credits to reduce our future U.S. federal income tax liability may be subject to limitations. This could result in increased U.S. federal income tax liability for us if we generate taxable income in a future period. Limitations on the use of NOLs and other tax attributes could also increase our state tax liability. Any such limitation could have a material adverse effect on our results of operations in future years. We have not completed a study to assess whether an ownership change for purposes of Section 382 or 383 has occurred, or whether there have been multiple ownership changes since our inception, due to the significant costs and complexities associated with such study.

The use of our tax attributes will also be limited to the extent that we do not generate positive taxable income in future tax periods. We do not expect to generate positive taxable income in the near future and we may never achieve tax profitability.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights.

We may seek additional capital through a combination of private and public equity offerings, debt financings, collaborations and strategic and licensing arrangements. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, a stockholder's ownership interest in our company will be diluted. In addition, the terms of any such securities may include liquidation or other preferences that materially adversely affect the rights of our stockholders. Debt financing, if available, would increase our fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaboration, strategic partnerships and licensing arrangements with third parties, we may have to relinquish valuable rights to setmelanotide, our intellectual property or future revenue streams, or grant licenses on terms that are not favorable to us.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

If those stockholders who hold shares of our common stock immediately prior to the effectiveness of the registration statement of which this prospectus forms a part sell, or indicate an intention to sell, substantial amounts of our common stock in the public market after the lock-up and other legal restrictions on resale discussed in this prospectus lapse, the market price of our common stock could decline and our ability to raise adequate capital through the sale of additional equity securities could be impaired. Upon completion of this offering, there will be 25,843,306 shares of our common stock outstanding, assuming no exercise of the underwriters' option to purchase additional shares of common stock. Of these shares, as of the date of this prospectus, approximately 6.7 million shares of our common stock, plus any shares sold upon exercise of the underwriters' option to purchase additional shares of common stock, will be freely tradable, without restriction, in the public market immediately following this offering, except for shares purchased by affiliates, and the remaining shares may be sold upon expiration of the lock-up agreements pertaining to this offering 180 days after the date of this offering, subject in some cases to volume limitations. The representatives of the underwriters, however, may, in their sole discretion, permit our officers, directors and other stockholders who are subject to these lock-up agreements to sell shares prior to the expiration of the lock-up agreements.

After this offering, the holders of approximately 18,858,976 shares of our common stock will be entitled to rights with respect to the registration of their shares under the Securities Act of 1933, as amended, or the Securities Act, subject to the lock-up agreements described above, including requiring us to file registration statements covering the shares of our common stock they hold or to include their shares in registration statements that we may file for ourselves or other stockholders. See "Description of Capital Stock—Registration Rights" in this prospectus for more information regarding these registration rights. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these stockholders could have a material adverse effect on the market price of our common stock. These registration rights have been waived in connection with this offering.

We also intend to register all the shares of common stock that we may issue under our equity incentive plans. Effective upon the effectiveness of the registration statement of which this prospectus is a part, an aggregate of 4,276,971 shares of our common stock will be reserved for future issuance under these plans. Once we register these shares, which we plan to do shortly after the completion of this offering, they can be freely sold in the public market upon issuance, subject to the lock-up agreements referred to above. If a large number of these shares are sold in the public market, the sales could reduce the trading price of our common stock. See "Shares Eligible for Future Sale" for a more detailed description of sales that may occur in the future.

We are an "emerging growth company," and as a result of the reduced disclosure and governance requirements applicable to emerging growth companies, our common stock may be less attractive to investors.

We are an "emerging growth company" as defined in the JOBS Act, and we intend to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, or Section 404, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. If we choose not to comply with the auditor attestation requirements of Section 404, our auditors will not be required to attest to the effectiveness of our internal control over financial reporting. As a result, investors may become less comfortable with the effectiveness of our internal controls and the risk that material weaknesses or other deficiencies in our internal controls go undetected or may increase. If we choose to provide reduced disclosures in our periodic reports and proxy statements while we are an emerging growth company, investors would have access to less information and analysis about our executive compensation, which may make it difficult for investors to evaluate our executive compensation practices. We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an "emerging growth company." We will remain an "emerging growth company" until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of this offering, (b) in which we have total annual gross revenue of at least \$1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior June 30th, and (2) the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period.

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporation governance policies.

As a public company, and particularly after we are no longer an emerging growth company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, or Sarbanes-Oxley, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the NASDAQ Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors.

We are evaluating these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

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For as long as we remain an emerging growth company, we may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not applicable to emerging growth companies as described in the preceding risk factor.

Pursuant to Section 404 of Sarbanes-Oxley, we will be required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses in our internal control over financial reporting, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

We may be at an increased risk of securities class action litigation.

Historically, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years. If we were to be sued, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

We do not intend to pay dividends on our common stock and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of our common stock.

We have never declared or paid any cash dividends on our common stock and do not currently intend to do so in the foreseeable future. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends in the foreseeable future. Therefore, the success of an investment in shares of our common stock will depend upon any future appreciation in their value. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which you purchased them.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements, which reflect our current views with respect to, among other things, our operations and financial performance. You can identify these forward-looking statements by the use of words such as "outlook," "believes," "expects," "potential," "continues," "may," "will," "should," "seeks," "approximately," "predicts," "intends," "plans," "estimates," "anticipates" or the negative version of these words or other comparable words. Such forward-looking statements are subject to various risks and uncertainties. Accordingly, there are or will be important factors that could cause actual outcomes or results to differ materially from those indicated in these statements. We believe these factors include but are not limited to those described under "Risk Factors" and include, among other things:

- the success, cost and timing of our product development activities and clinical trials;
- our ability to obtain and maintain regulatory approval for setmelanotide and our future product candidates, if any, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- our ability to obtain funding for our operations;
- the commercialization of setmelanotide, if approved;
- the number of people in our target patient population;
- our plans to research, develop and commercialize setmelanotide;
- our ability to operate, and the implementation of our business strategy, as an independent company;
- our ability to attract collaborators with development, regulatory and commercialization expertise;
- our expectations regarding our ability to obtain and maintain intellectual property protection for setmelanotide;
- future agreements with third parties in connection with the commercialization of setmelanotide or our future product candidates, if any;
- the size and growth potential of the markets for setmelanotide, and our ability to serve those markets;
- our expectations for the pricing of setmelanotide;
- the rate and degree of market acceptance of setmelanotide, as well as the reimbursement coverage for setmelanotide;
- regulatory developments in the United States, the European Union and other jurisdictions;
- the performance of our third-party suppliers and manufacturers;
- the extent and success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- the accuracy of our estimates regarding our target patient populations, expenses, future revenues, capital requirements and needs for additional financing;
- our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act; and
- our use of the proceeds from this offering.

These factors should not be construed as exhaustive and should be read in conjunction with the other cautionary statements that are included in this prospectus. We undertake no obligation to publicly update or review any forward-looking statement, whether as a result of new information, future developments or otherwise.

MARKET, INDUSTRY AND OTHER DATA

This prospectus includes market, industry and other data and forecasts that we have derived from independent consultant reports, publicly available information, various industry publications, other published industry sources and our internal data and estimates. Independent consultant reports, industry publications and other published industry sources generally indicate that the information contained therein was obtained from sources believed to be reliable.

Due to the rarity of our target indications, there is no available comprehensive patient registry or other method of establishing with precision the actual number of patients with MC4 pathway genetic defects. As a result, we have had to rely on other available sources to derive prevalence estimates for our target indications. Since the published epidemiology studies for these disorders are based on relatively small population samples, and are not amenable to robust statistical analyses, it is possible that these projections may exceed the addressable population, particularly given the need to genotype patients to definitively confirm a diagnosis.

We have estimated the potential addressable patient populations with these disorders based on the following sources and assumptions:

- *POMC Deficiency Obesity.* There are approximately 50 patients with POMC deficiency obesity noted in a series of published case reports, each mostly reporting a single or small number of patients. However, we believe our addressable patient population for this deficiency may be approximately 100 to 500 patients in the United States, and a comparable addressable patient population in Europe, as most of the reported cases are from a small number of academic research centers, and because genetic testing for POMC deficiency is often unavailable and currently is rarely performed. Based on discussions with experts in rare diseases, we also believe the number of diagnosed cases could increase several-fold with increased awareness of this deficiency and the availability of new treatments.
- *LepR Deficiency Obesity and POMC Heterozygous Deficiency Obesity.* Our addressable patient population estimate for LepR deficiency obesity is approximately 500 to 2,000 patients in the United States, and for POMC heterozygous deficiency obesity is approximately 4,000 patients in the United States, with a comparable addressable patient population for both indications in Europe. Our estimates are based on:
 - epidemiology studies on LepR deficiency and POMC heterozygous deficiency in small cohorts of patients comprised of children with severe obesity and adults with severe obesity who have a history of early onset obesity;
 - U.S. Census Bureau figures for adults and children, and Centers for Disease Control and Prevention, or CDC, prevalence numbers for severe adult obese patients (BMI greater than 40 kg/ m²) and for severe early onset obese children (99th percentile at ages two to 17 years old); and
 - with wider availability of genetic testing expected for LepR deficiency and POMC heterozygous deficiency and increased awareness of new treatments, our belief that up to 40% of patients with these disorders may eventually be diagnosed.

Using these sources and assumptions, we calculated our estimates for addressable populations by multiplying (x) our estimate of the number of patients comprised of children with severe obesity and our estimate of a projected number of adults with severe obesity who have a history of early onset obesity, (y) the estimated prevalence from epidemiology studies of approximately 1% for LepR deficiency and 2% for POMC heterozygous, and (z) our estimated diagnosis rate of up to 40%.

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- *Bardet-Biedl Syndrome.* Our addressable patient population estimate for Bardet-Biedl syndrome is approximately 1,500 to 2,500 patients in the United States based on:
 - Published prevalence estimates of one in 100,000 in North America, which projects to approximately 3,250 people in the United States. We believe the majority of these patients are addressable patients; and
 - We believe that with wider availability of genetic testing expected for Bardet-Biedl syndrome and increased awareness of new treatments, the number of patients diagnosed with this disorder will increase.
- *Alström Syndrome.* Our addressable patient population estimate for Alström syndrome is approximately 500 to 1,000 patients worldwide. This estimate is based on:
 - Published prevalence estimates of one in 1,000,000 in North America, which projects to approximately 325 people in the United States. We believe the majority of these patients are addressable patients; and
 - We believe that with wider availability of genetic testing expected for Alström syndrome and increased awareness of new treatments, the number of patients diagnosed with this disorder will increase.
- *POMC Epigenetic Disorders.* There is currently no epidemiology data that defines the prevalence of POMC epigenetic disorders.

We believe that the patient populations in the European Union are at least as large as those in the United States. However, we do not have comparable epidemiological data from the European Union and these estimates are therefore based solely on applying relative population percentages to the Company derived estimates described above.

We are conducting additional epidemiology studies to strengthen these prevalence projections. In parallel, we are also developing a patient registry for diagnosed patients with POMC deficiency and LepR deficiency which will further inform prevalence projections for these rare genetic orders. See "*Business—Other Clinical Initiatives in Genetic Obesity—Genotyping Study.*" for additional information.

See "*Risk Factors—Risks Related to the Development of Setmelanotide—The number of patients suffering from each of the MC4 pathway deficiencies we are targeting is small and has not been established with precision. If the actual number of patients is smaller than we estimate, our revenue and ability to achieve profitability may be materially adversely affected.*" for additional information.

USE OF PROCEEDS

We estimate that the net proceeds to us from the sale of the shares of our common stock offered by us will be approximately \$90.6 million, based on an assumed initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting underwriting discounts and commissions. If the underwriters' option to purchase additional shares in this offering is exercised in full, we estimate that our net proceeds will be approximately \$104.5 million, after deducting underwriting discounts and commissions.

A \$1.00 increase (decrease) in the assumed initial public offering price of \$15.00 per share would increase (decrease) the net proceeds to us from this offering by approximately \$6.2 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions. Similarly, each increase (decrease) of one million shares in the number of shares of common stock offered by us would increase (decrease) the net proceeds to us from this offering by approximately \$14.0 million, assuming the assumed initial public offering price remains the same and after deducting underwriting discounts and commissions.

As of June 30, 2017, we had cash and cash equivalents and short-term investments of approximately \$17.7 million and after giving effect, on a pro forma basis, to the aggregate gross proceeds of \$20.5 million from the sale of our series A preferred stock in August 2017, \$38.2 million. We intend to use the net proceeds from this offering, together with our existing cash resources, as follows:

- approximately \$17 million to fund the development and manufacturing of setmelanotide through completion of our Phase 3 clinical trials and subsequent NDA submissions with the FDA for the treatment of POMC deficiency obesity and LepR deficiency obesity;
- approximately \$14 million for the development of setmelanotide through completion of our Phase 2 proof of concept clinical trials for Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity and POMC epigenetic disorders, as well as the initiation of our Phase 3 clinical trial for Bardet-Biedl syndrome;
- approximately \$16 million for initiatives to expand the diagnosis of genetic obesity, including research and scientific exchange related to our ongoing genotyping and genetic epidemiology studies;
- approximately \$38 million for preparation for commercialization of setmelanotide; and
- the remainder for general working capital and administrative expenses, additional research and development expenses, and other general corporate purposes.

Our expected use of net proceeds from this offering represents our current intentions based upon our present plans and business condition. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the closing of this offering, or the amounts that we will actually spend on the uses set forth above. The amounts and timing of our actual use of the net proceeds will vary depending on numerous factors, including the progress of our clinical trials and other development efforts for setmelanotide and other factors described in "Risk Factors" beginning on page 16, as well as the amount of cash we use in our operations. As a result, our management will have broad discretion in the application of the net proceeds, and investors will be relying on our judgment regarding the application of the net proceeds of this offering. In addition, we might decide to postpone or not pursue clinical trials or preclinical activities if the net proceeds from this offering and the other sources of cash are less than expected.

Pending application of the net proceeds, we intend to invest the net proceeds from this offering in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government. We may still require significant additional capital to fund the continued development of setmelanotide and our operating needs thereafter. We expect to finance our additional cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements.

DIVIDEND POLICY

We currently intend to retain all available funds and any future earnings for use in the operation of our business and do not anticipate paying any dividends on our common stock in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general business conditions and other factors that our board of directors may deem relevant.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and short-term investments and capitalization as of June 30, 2017, as follows:

- on an actual basis;
- on a pro forma basis to reflect the issuance of 78,666,209 shares of our series A-1 junior preferred stock in exchange for 8,578,646 shares of our common stock in connection with the Distribution, the issuance of additional shares of series A preferred stock in August 2017 for gross proceeds of \$20.5 million (see Note 12 within the notes to our financial statements appearing elsewhere in this prospectus) and the conversion of all of our outstanding preferred stock into 17,406,338 shares of common stock upon the closing of this offering and;
- on a pro forma as adjusted basis to give further effect to the issuance and sale of 6,666,666 shares of our common stock in this offering at an assumed initial public offering price of \$15.00 per share, which is the midpoint of the price range listed on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Our capitalization following the closing of this offering will be adjusted based on the actual initial public offering price and other terms of the offering determined at pricing. You should read this information in conjunction with our financial statements and the related notes appearing at the end of this prospectus, the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section and other financial information contained in this prospectus. You should also read this table together with the information contained in this prospectus, including "Use of Proceeds," and the historical financial statements and related notes included elsewhere in this prospectus.

	As of June 30, 2017		
	Actual	Pro Forma (unaudited) (in thousands)	Pro Forma As Adjusted
Cash and cash equivalents and short-term investments	\$ 17,740	\$ 38,215	\$ 128,815
Convertible preferred stock:			
Series A preferred stock; 80,950,000 shares authorized; 60,475,001 shares issued and outstanding actual; no shares issued and outstanding pro forma and pro forma as adjusted	60,147	—	—
Stockholders' equity (deficit):			
Common stock, \$0.001 par value; 21,341,330 shares authorized, 10,196,292 shares issued and outstanding actual; 19,023,984 shares issued and outstanding pro forma; and 25,690,650 shares issued and outstanding pro forma as adjusted	10	19	26
Additional paid-in capital	44,429	125,452	216,045
Accumulated deficit	(89,705)	(89,705)	(89,705)
Total stockholders' equity (deficit)	<u>(45,266)</u>	<u>35,766</u>	<u>126,366</u>
Total capitalization	<u>\$ 14,881</u>	<u>\$ 35,766</u>	<u>\$ 126,366</u>

The information above is illustrative only and our capitalization following the completion of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing.

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A \$1.00 increase (decrease) in the assumed initial public offering price of \$15.00 per share, the midpoint of the estimated price range shown on the cover page of this prospectus, would increase (decrease) the amount of cash and cash equivalents, additional paid-in capital, total stockholders' equity (deficit) and total capitalization on a pro forma as adjusted basis by approximately \$6.2 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase (decrease) of one million shares offered by us would increase (decrease) cash and cash equivalents, total stockholders' equity (deficit) and total capitalization on a pro forma as adjusted basis by approximately \$14.0 million, assuming the assumed initial public offering price remains the same, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. A one million share increase in the number of shares offered by us together with a concomitant \$1.00 increase in the assumed initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase each of cash and cash equivalents and total stockholders' (deficit) equity by approximately \$21.1 million after deducting underwriting discounts and commissions and estimated offering expenses payable by us. Conversely, a one million share decrease in the number of shares offered by us together with a concomitant \$1.00 decrease in the assumed initial public offering price of \$15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, would decrease each of cash and cash equivalents and total stockholders' (deficit) equity by approximately \$19.2 million after deducting underwriting discounts and commissions and estimated offering expenses payable by us. The pro forma as adjusted information discussed above is illustrative only and will be adjusted based on the actual public offering price and other terms of this offering determined at pricing.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the initial public offering price per share and the pro forma as adjusted net tangible book value per share of our common stock after this offering.

Our historical net tangible book value as of June 30, 2017 was approximately \$(45.3) million, or \$(4.44) per share of our common share. Our historical net tangible book value represents our total tangible assets less our total liabilities. Net historical tangible book value per common share is our historical net tangible book value divided by the number of common shares outstanding as of June 30, 2017.

Our pro forma net tangible book value as of June 30, 2017 was approximately \$35.8 million, or \$1.88 per share of our common stock. Pro forma net tangible book value represents our total tangible assets less our total liabilities, after giving effect to (1) to reflect the issuance of 78,666,209 shares of our series A-1 junior preferred stock in exchange for 8,578,646 shares of our common stock in connection with the Distribution, (2) our sale of 20,474,998 shares of series A preferred stock in August 2017 for gross proceeds of \$20.5 million and (3) the conversion of all outstanding shares of our preferred stock into 17,406,338 shares of common stock upon the closing of this offering. Pro forma net tangible book value per share represents pro forma net tangible book value divided by the total number of common shares outstanding as of June 30, 2017 after giving effect to the pro forma adjustments described above.

Our pro forma as adjusted net tangible book value represents our pro forma net tangible book value, plus the effect of the issuance and sale of 6,666,666 shares of our common stock in this offering at an assumed initial public offering of \$15.00 per share (the midpoint of the price range set forth on the cover page of this prospectus), after deducting underwriting discounts and commissions and estimating offering expenses payable by us. Pro forma as adjusted net tangible book value per share represents pro forma as adjusted net tangible book value divided by the total number of common shares outstanding as of June 30, 2017, after giving effect to the pro forma adjustments and the offering described above. Our pro forma as adjusted net tangible book value as of June 30, 2017 was approximately \$126.4 million, or \$4.92 per share of our common stock. This amount represents an immediate increase in the pro forma adjusted net tangible book value of \$3.04 per share to existing shareholders and an immediate dilution of \$10.08 per share to new investors purchasing shares at an assumed initial public offering price of \$15.00 per share (the midpoint of the price range set forth on the cover page of this prospectus).

The following table illustrates this dilution on a per share basis:

Assumed initial public offering price per share	\$ 15.00
Historical net tangible book value per share as of June 30, 2017	\$ (4.44)
Increase per share attributable to pro forma adjustments described above	6.32
Pro forma net tangible book value per share at June 30, 2017	\$ 1.88
Increase per share attributable to new investors	3.04
Pro forma as adjusted net tangible book value per share at June 30, 2017 after giving effect to the offering	4.92
Dilution per share to new investors	\$ 10.08

A \$1.00 increase (decrease) in the assumed initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted net tangible book value per share after this offering by approximately \$0.24 per share and the dilution per share to investors participating in this offering by approximately \$0.76 per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us.

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The following table summarizes, on a pro forma basis as of June 30, 2017, the total number of shares purchased from us, the total consideration paid, or to be paid, and the average price per share paid, or to be paid, by existing stockholders and by new investors in this offering at an assumed initial public offering price of \$15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. As the table below shows, new investors purchasing shares in this offering will pay an average price per share substantially higher than our existing stockholders paid.

	Shares Purchased		Total Consideration		Average Price Per Share
	Number	Percentage	Amount (in thousands)	Percentage	
Existing stockholders	19,023,984	74%	\$ 81,043	45%	\$ 4.26
New investors(1)	6,666,666	26%	100,000	55%	15.00
Total	25,690,650	100%	\$ 181,043	100%	\$ 7.05

- (1) Certain of our existing principal stockholders, directors and their affiliated entities, have indicated an interest in purchasing an aggregate of approximately \$40.0 million in shares of our common stock in this offering at the initial public offering price per share and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers, and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering. The presentation in this table regarding ownership by existing principal stockholders does not give effect to any purchases in this offering by such potential purchasers.

Except as otherwise indicated, the discussion and tables above assume no exercise of the underwriters' option to purchase additional shares of our common stock in this offering. If the underwriters' option to purchase additional shares is exercised in full:

- the percentage of outstanding common stock held by existing stockholders will be reduced to 71% of the total number of shares of common stock to be outstanding upon completion of this offering; and
- the number of shares of common stock held by investors participating in this offering will be increased to 7,666,666 shares, or 29% of the total number of shares of common stock to be outstanding upon completion of this offering.

Effective immediately upon closing of this offering, an aggregate of 4,018,538 shares of our common stock will be reserved for issuance under our 2017 equity incentive plan, or the 2017 Plan, and an aggregate of 258,433 shares of our common stock will be reserved for issuance under our 2017 employee stock purchase plan. Furthermore, we may choose to raise additional capital through the sale of equity or convertible debt securities due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that any new options are issued under our equity incentive plans or we issue additional shares of common stock or other equity or convertible debt securities in the future, there will be further dilution to investors participating in this offering.

SELECTED FINANCIAL DATA

The following selected statements of operations data for the years ended December 31, 2015 and 2016 and the balance sheet data as of December 31, 2015 and 2016 are derived from our audited financial statements appearing elsewhere in this prospectus. The selected statements of operations data for the six months ended June 30, 2016 and 2017 and the balance sheet data as of June 30, 2017 have been derived from our unaudited financial statements included elsewhere in this prospectus. In our opinion, these unaudited financial statements have been prepared on a basis consistent with our audited financial statements and contain all adjustments, consisting only of normal and recurring adjustments, necessary for a fair presentation of such financial data. In our opinion, you should read this data together with our audited financial statements and related notes appearing elsewhere in this prospectus and the information under the caption "Management's Discussion and Analysis of Financial Condition and Results of Operations."

Our financial statements for the periods presented include allocations of costs from certain shared functions provided to us by the Relamorelin Company. These allocations were made based on either a specific identification basis or, when specific identification is not practicable, a proportional cost allocation method which allocates expenses based on the percentage of employee time and research and development effort expended on our business as compared to total employee time and research and development effort, and have been included in our financial statements for the periods presented.

The financial statements included in this prospectus may not necessarily reflect our financial position, results of operations and cash flows as if we had operated as an independent company during all of the periods presented. See "Summary—Corporate Reorganization."

Our historical results are not necessarily indicative of our future results, and our operating results for the six-month period ended June 30, 2017 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2017 or any other interim periods or any future year or period.

	Year Ended December 31, 2015	Year Ended December 31, 2016	Six Months Ended June 30, 2016	2017
	(in thousands, except share and per share data)			
Operating expenses:				
Research and development	\$ 7,148	\$ 19,594	\$ 8,544	\$ 10,270
General and administrative	<u>3,425</u>	<u>6,311</u>	<u>2,585</u>	<u>2,873</u>
Total operating expenses	<u>10,573</u>	<u>25,905</u>	<u>11,129</u>	<u>13,143</u>
Loss from operations	<u>(10,573)</u>	<u>(25,905)</u>	<u>(11,129)</u>	<u>(13,143)</u>
Other income (expense):				
Revaluation of Series A Investor Right/Obligation and Series A Investor Instrument	(500)	—	—	(82)
Interest income, net	<u>—</u>	<u>33</u>	<u>14</u>	<u>63</u>
Total other income (expense):	<u>(500)</u>	<u>33</u>	<u>14</u>	<u>(19)</u>
Net loss and comprehensive loss	<u>\$ (11,073)</u>	<u>\$ (25,872)</u>	<u>\$ (11,115)</u>	<u>\$ (13,162)</u>
Net loss attributable to common stockholders	<u>\$ (12,000)</u>	<u>\$ (29,074)</u>	<u>\$ (12,711)</u>	<u>\$ (15,534)</u>
Net loss attributable to common stockholders per common share, basic and diluted(1)	<u>\$ (1.18)</u>	<u>\$ (2.85)</u>	<u>\$ (1.25)</u>	<u>\$ (1.52)</u>
Weighted average common shares outstanding, basic and diluted	<u>10,196,292</u>	<u>10,196,292</u>	<u>10,196,292</u>	<u>10,196,292</u>
Pro forma net loss attributable to common stockholders per common share, basic and diluted (unaudited)(1)(2)	<u>\$ (1.78)</u>			<u>\$ (0.79)</u>
Pro forma weighted average common shares outstanding, basic and diluted (unaudited)(1)(2)	<u>14,558,342</u>			<u>16,729,487</u>

	December 31, 2015	December 31, 2016	June 30, 2017
Balance Sheet Data:			
Cash, cash equivalents and short-term investments	\$ 34,869	\$ 10,537	\$ 17,740
Working capital (deficit)	30,218	6,444	13,619
Total assets	37,275	12,339	20,404
Convertible preferred stock	40,000	40,000	60,147
Accumulated deficit	(50,671)	(76,543)	(89,705)
Total stockholders' equity (deficit)	\$ (7,999)	\$ (32,703)	\$ (45,266)

- (1) See Note 2 within the notes to our financial statements appearing elsewhere in this prospectus for a description of the methods used to calculate basic and diluted net loss per share and pro forma basic and diluted net loss per share.
- (2) Pro forma to reflect the issuance of 78,666,209 shares of our series A-1 junior preferred stock in exchange for 8,578,646 shares of our common stock in connection with the Distribution, the issuance of additional shares of series A preferred stock in August 2017 (see Note 12 within the notes to our financial statements appearing elsewhere in this prospectus) and the conversion of all of our outstanding preferred stock into 17,406,338 shares of common stock upon the closing of this offering.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and the related notes and other financial information included elsewhere in this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those set forth in the "Risk Factors" section of this prospectus, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a biopharmaceutical company focused on the development and commercialization of peptide therapeutics for the treatment of rare genetic deficiencies that result in life-threatening metabolic disorders. Our lead peptide product candidate is setmelanotide, a potent, first-in-class MC4R agonist for the treatment of rare genetic disorders of obesity. We believe setmelanotide, for which we have exclusive worldwide rights, has the potential to serve as replacement therapy for the treatment of MC4 pathway deficiencies. Our development efforts are initially focused on obesity related to six monogenic MC4 pathway deficiencies, POMC, LepR, Bardet-Biedl syndrome, Alström syndrome POMC heterozygous and POMC epigenetic disorders, for which there are currently no effective or approved treatments. We believe that the MC4 pathway is a compelling target for treating these genetic disorders because of its critical role in regulating appetite and weight by promoting satiety and weight control, and that peptide therapeutics are uniquely suited for activating this target. We have demonstrated proof of concept in Phase 2 clinical trials in POMC deficiency obesity, LepR deficiency obesity and Bardet-Biedl syndrome, three of these genetic disorders of extreme and unrelenting appetite and obesity, in which setmelanotide dramatically reduced both weight and hunger. We are currently enrolling patients in a Phase 3 clinical trial for POMC deficiency obesity and expect to enroll the first patient in a Phase 3 clinical trial for LepR deficiency obesity in the second half of 2017. We recently demonstrated preliminary proof of concept in our Phase 2 clinical trial in Bardet-Biedl syndrome, indicating that this is also a setmelanotide-responsive, upstream MC4 pathway disorder. We are continuing to enroll patients in this trial and expect to report preliminary Phase 2 results in the fourth quarter of 2017. We expect to initiate a Phase 3 clinical trial in Bardet-Biedl syndrome in 2018. We have also initiated Phase 2 clinical trials in Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders.

We have leveraged skilled experts, consultants, Contract Research Organizations, or CROs, and contractors to manage our clinical operations under the leadership and direction of our management. We expect to expand our infrastructure to manage our clinical, finance and commercial operations with a higher proportion of full-time employees. We have fifteen employees, four of whom hold Ph.D. or M.D. degrees. Of these employees, ten are engaged in development and commercialization activities and five are engaged in support administration, including business development and finance. In the near-term, we expect to significantly expand our clinical and finance personnel, in particular, and will incur increased expenses as a result.

Our operations to date have been limited primarily to conducting research and development activities for setmelanotide. To date, we have not generated any product revenue and have financed our operations primarily through capital contributions from the Predecessor Company, the Relamorelin Company and the LLC entity and, more recently, the private placement of equity securities to outside investors. We will not generate revenue from product sales until we successfully complete development and obtain regulatory approval for setmelanotide, which we expect will take a number of years and is subject to significant uncertainty. We expect to continue to fund our operations through the sale of equity, debt financings or other sources. We intend to build our own marketing and commercial sales infrastructure and we may

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enter into collaborations with other parties for certain markets outside the United States. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such other arrangements as, and when, needed, we may have to significantly delay, scale back or discontinue the development or commercialization of setmelanotide. See "Risk Factors—*Risks Related to Our Financial Position and Need for Capital*" beginning on page 16 of this prospectus for additional information.

As of June 30, 2017, we had an accumulated deficit of \$89.7 million. Our net losses were \$11.1 million and \$25.9 million for the year ended December 31, 2015 and 2016, respectively, and \$11.1 million and \$13.2 million for the six months ended June 30, 2016 and 2017, respectively. We expect to continue to incur significant expenses and increasing operating losses over the foreseeable future. We expect our expenses will increase substantially in connection with our ongoing activities, as we:

- continue to conduct clinical trials for setmelanotide;
- engage CMOs for the manufacture of setmelanotide for clinical trials;
- seek regulatory approval for setmelanotide;
- expand our clinical and financial operations and build a marketing and commercialization infrastructure; and
- operate as a public company.

As of June 30, 2017, our existing cash and cash equivalents and short-term investments were approximately \$17.7 million and after giving effect, on a pro forma basis, to the aggregate gross proceeds from the sale of our series A preferred stock in August 2017, \$38.2 million. We expect that the net proceeds of this offering will enable us to fund our operating expenses into the first half of 2019.

Corporate Background and Distribution

We are a Delaware corporation organized in February 2013 under the name Rhythm Metabolic, Inc., and as of October 2015, under the name Rhythm Pharmaceuticals, Inc. Prior to our organization and the Corporate Reorganization, we were part of the Predecessor Company which commenced active operations in 2010. As a result of the Corporate Reorganization, we became a wholly-owned subsidiary of the LLC entity. In August 2015, December 2015, January 2017 and August 2017, we sold shares of our series A preferred stock to investors pursuant to an equity financing.

In August 2017, the LLC entity exchanged 8,578,646 of its shares of our common stock for 78,666,209 of newly-issued shares of our series A-1 junior preferred stock, which will be converted into our common stock on 9.17-for-1 basis upon the closing of this offering, and the LLC entity distributed all of its shares of our series A-1 junior preferred stock and common stock to its members.

In connection with this offering, we will effect a 1-for-9.17 reverse stock split of our outstanding common stock.

We shared certain costs with the Relamorelin Company and effective December 2016 in connection with the sale of the Relamorelin Company, we no longer share these costs.

Financial Operations Overview

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of setmelanotide for at least several years. We cannot predict if, when, or to what extent we will generate revenues from the commercialization and sale of setmelanotide. Setmelanotide is currently our only product candidate, and we may never succeed in achieving regulatory approval for setmelanotide or any other product candidate that we decide to pursue in the future.

Research and development expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our drug discovery efforts, and the development of setmelanotide, which include:

- expenses incurred under agreements with third parties, including CROs that conduct research and development and preclinical activities on our behalf, and the cost of consultants and CMOs that manufacture drug products for use in our preclinical studies and clinical trials;
- employee-related expenses including salaries, benefits, and stock-based compensation expense;
- the cost of lab supplies and acquiring, developing, and manufacturing preclinical study materials; and
- facilities, depreciation, and other expenses, which include rent and maintenance of facilities, insurance and other operating costs.

We expense research and development costs to operations as incurred. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

The following table summarizes our current research and development program for setmelanotide.

Research and Development Summary	Year Ended December 31,		Six Months Ended June 30,	
	2015	2016	2016	2017
Setmelanotide Program	\$ 7,148	\$ 19,594	\$ 8,544	\$ 10,270

We are unable to predict the duration and costs of the current or future clinical trials of setmelanotide. The duration, costs, and timing of clinical trials and development of setmelanotide will depend on a variety of factors, including:

- the scope, rate of progress, and expense of our ongoing, as well as any additional, clinical trials and other research and development activities;
- the rate of enrollment in clinical trials;
- the safety and efficacy demonstrated by setmelanotide in future clinical trials;
- changes in regulatory requirements;
- changes in clinical trial design; and
- the timing and receipt of any regulatory approvals.

A change in the outcome of any of these variables with respect to the development of setmelanotide would significantly change the costs and timing associated with its development and potential commercialization.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect research and development costs to increase significantly for the foreseeable future as our setmelanotide development program progresses. However, we do not believe that it is possible at this time to accurately project total program-specific expenses to commercialization and there can be no guarantee that we can meet the funding needs associated with these expenses.

General and administrative expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, relating to our full-time employees and until December 2016, for personnel which have been allocated from the Relamorelin Company. Other significant costs include rent which previously had been allocated from the Relamorelin Company, legal fees relating to patent and corporate matters and fees for accounting and consulting services.

The following table summarizes our current general and administrative expenses.

	Year Ended December 31,		Six Months Ended June 30,	
	2015	2016	2016	2017
General and administrative expense	\$ 3,425	\$ 6,311	\$ 2,585	\$ 2,873

We anticipate that our general and administrative expenses will increase in the future to support continued and expanding development efforts, potential commercialization of setmelanotide and increased costs of operating as a public company. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, lawyers and accountants, compliance with exchange listing and SEC expenses, insurance and investor relations costs, among other expenses.

Critical Accounting Policies and Estimates

Our discussion and analysis of our financial condition and results of operations are based on our financial statements, which we have prepared in accordance with United States generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported amounts of revenues and expenses during the reporting periods. On an ongoing basis, we evaluate our estimates and judgments, including those described in greater detail below. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our financial statements included elsewhere in this prospectus, we believe that the following accounting policies are the most critical to aid in fully understanding and evaluating our financial condition and results of operations.

Basis of Presentation**Presentation**

We have historically existed and functioned as part of the consolidated businesses of the Predecessor Company. Our MC4 business was contributed to us from the Predecessor Company on March 21, 2013 as part of the Corporate Reorganization. At that time, we also entered into the Payroll Services Agreement. In December 2016, the shared employees terminated their existing employment agreements and entered into new agreements with us. Until December 2016, we shared costs with the Relamorelin Company, including finance, accounting, research and development and operations. These shared costs were allocated to us from the Relamorelin Company for the purposes of preparing the financial statements based on a specific identification basis or, when specific identification is not practicable, a proportional cost allocation method which allocates expenses based upon the percentage of employee time and research and development effort expended on our business as compared to total employee time and research and development effort. The proportional use basis adopted to allocate shared costs is in accordance with the

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guidance of Staff Accounting Bulletin Topic 1B. Our management has determined that the proportional use method of allocating costs to us from the Relamorelin Company is reasonable.

Accrued research and development expenses

As part of the process of preparing our financial statements, we are required to estimate the value associated with goods and services received in the period in connection with research and development activities. This process involves reviewing quotations and contracts, identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost, or alternatively, the deferral of amounts paid for goods or services to be incurred in the future. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses or prepaid expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at the time those financial statements are prepared. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include fees paid to CROs and CMOs in connection with research and development activities.

We accrue our expenses related to CROs and CMOs based on our estimates of the services received and efforts expended pursuant to quotes and contracts with CROs and CMOs that conduct research and development and manufacturing on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. The allocation of CRO upfront expenses for both clinical trials and preclinical studies generally tracks actual work activity. However, there may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees delivered over a period of time, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust accrued or prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

2015 Series A Investor Right/Obligation, 2015 Series A Investor Call Option & 2017 Series A Investor Instrument

Pursuant to the 2015 series A stock purchase agreement, by and among us and the other persons that are parties to such agreement as investors, or the series A investors, we issued 25,000,000 shares of series A preferred stock at a purchase price of \$1.00 per share in August 2015 as part of an initial tranche of financing. Pursuant to the series A stock purchase agreement, the series A investors had the obligation, or the 2015 Series A Investor Right/Obligation, to purchase additional shares of series A preferred stock as part of a second tranche of financing based on the achievement of a specific milestone set forth in the series A preferred stock purchase agreement, or the 2015 Second Tranche Milestone. Additionally, subject to the terms and conditions set forth in the series A stock purchase agreement, the series A investors had the option, or the 2015 Series A Investor Call Option, to purchase 15,000,000 additional shares of series A preferred stock in the event that the 2015 Second Tranche Milestone was not achieved. The 2015 Series A Investor Right/Obligation was exercised and the 2015 Series A Investor Call Option expired on December 1, 2015 upon the 2015 Series A Second Tranche Closing. As a result of these two tranches, we issued 40,000,000 shares of series A preferred stock resulting in aggregate gross proceeds of \$40.0 million.

Pursuant to the 2017 series A preferred stock purchase agreement, by and among us and certain purchasers, and as part of an initial tranche closing, we issued 20,475,001 shares of series A preferred stock

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at a purchase price of \$1.00 per share in January 2017. The series A stock purchase agreement provided for the delayed issuance by us of up to an additional 20,474,998 shares of series A preferred stock as part of a second tranche closing at a purchase price of \$1.00 per share. The series A investors had the obligation, upon notification by us, or the 2017 Series A Investor Right/Obligation, to purchase 20,474,998 additional shares of series A preferred stock as part of a second tranche of financing at such time as: (1) our cash, cash equivalents and short-term investments balance, net of accounts payable and accrued liabilities, falling below \$5.0 million and (2) our satisfaction of contractual and customary representations and warranties, or the 2017 Second Tranche Milestone. On August 18, 2017, the series A investors waived the \$5.0 million cash balance requirement of the 2017 second tranche milestone and such second tranche financing was consummated. As a result of these two tranches, we issued 40.95 million shares of our series A preferred stock, resulting in aggregate gross proceeds of \$40.95 million.

We have classified our 2015 Series A Investor Right/Obligation, our 2015 Series A Investor Call Option and our 2017 Series A Investor Instrument as liabilities as they are free-standing financial instruments. The 2015 Series A Investor Right/Obligation, the 2015 Series A Investor Call Option and the 2017 Series A Investor Instrument were recorded at fair value upon the issuance of our series A preferred stock in August 2015 and January 2017, respectively, and subsequently remeasured to fair value at each reporting period. Changes in fair value of these financial instruments are recognized as a component of other income (expense), net in the statement of operations and comprehensive loss. We estimated the fair value of the Series A Investor Right/Obligations as the probability-weighted present value of the expected benefit of the investment.

We used the Black-Scholes option-pricing model, which incorporates assumptions and estimates, to value the Series A Investor Call Options and assessed these assumptions and estimates on a quarterly basis as additional information impacting the assumptions was obtained. Estimates and assumptions impacting the fair value measurement include the fair value per share of the underlying series A preferred stock, the expected term of the Series A Investor Call Options, risk-free interest rate, expected dividend yield and expected volatility of the price of the underlying preferred stock. We determined the fair value per share of the underlying preferred stock by taking into consideration the most recent sale of our convertible preferred stock and the investors' right to invest in a subsequent tranche. As we are a private company and lack company-specific historical and implied volatility information of our stock, we estimated our expected stock volatility based on the historical volatility of publicly traded peer companies for a term comparable to the estimated term of the Series A Investor Call Options. The risk-free interest rate was determined by reference to the U.S. Treasury yield curve for time periods approximately equal to the estimated term of the Series A Investor Call Options. A dividend yield of zero was assumed. The fair value of the Series A Investor Instrument is determined to be the sum of the fair values of the 2017 Series A Investor Right/Obligation and the 2017 Investor Call Option.

Upon the closing of an initial public offering with a minimum price per share and gross proceeds of at least \$1.00, as adjusted for any splits or similar changes, and \$50.0 million, respectively, our series A preferred stock will automatically convert into shares of our common stock on a 9.17-for-1 basis.

Income taxes

Income taxes have been calculated on a separate tax return basis. Certain of our activities and costs have been included in the tax returns filed by the Relamorelin Company and the LLC entity. Prior to the Corporate Reorganization, our operations were included in the tax returns filed by the Predecessor Company. We have filed tax returns on our own behalf since the Corporate Reorganization.

We account for uncertain tax positions in accordance with the provisions of Accounting Standards Codification, or ASC, Topic 740, *Accounting for Income Taxes*, or ASC 740. When uncertain tax positions exist, we recognize the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based

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upon the technical merits of the tax position as well as consideration of the available facts and circumstances. As of December 31, 2016, we do not have any uncertain tax positions.

Income taxes are recorded in accordance with ASC 740, which provides for deferred taxes using an asset and liability approach. We recognize deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. We determine our deferred tax assets and liabilities based on differences between financial reporting and tax bases of assets and liabilities, which are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. Valuation allowances are provided, if based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

Interest and penalties on uncertain tax positions are recorded in the provision (benefit) for income taxes in the statements of operations. During the years ended December 31, 2015 and 2016 and the six months ended June 30, 2016 and 2017, we had no amounts accrued for interest and penalties related to uncertain tax positions.

As of December 31, 2016, we had net operating loss carryforwards to reduce federal and state incomes taxes of approximately \$46,934 and \$24,432, respectively. If not utilized, these carryforwards begin to expire in 2033. At December 31, 2016, we also had available research and development tax credits for federal and state income tax purposes of approximately \$971 and \$369, respectively. The federal and state credits begin to expire in 2033 and 2028, respectively.

Utilization of the net operating loss and tax credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that have occurred previously or that could occur in the future, as provided by Section 382 of the Code, or Section 382, as well as similar state provisions and other provisions of the Code. Ownership changes may limit the amount of net operating losses and tax credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an ownership change, as defined by Section 382, results from transactions that increase the ownership of 5.0% stockholders in the stock of a corporation by more than 50% in the aggregate over a three-year period.

Stock-based compensation

Prior to August 2015, we did not have our own equity compensation plan. In August 2015, our Board of Directors and our stockholders approved and we adopted the 2015 equity incentive plan, as amended and in effect prior to the closing of this offering, or the 2015 Plan, which we expect to terminate upon consummation of this offering and replace with the 2017 Plan. The 2015 Plan provides for the grant of incentive and non-qualified stock options and restricted stock and stock grants to employees, consultants, advisors and directors, as determined by the Board of Directors. We have reserved 2,317,339 shares of common stock under the 2015 Plan. The first option grants issued by us under the 2015 Plan were issued in the fourth quarter of 2015. Shares of common stock issued upon exercise of stock options are generally issued from authorized but unissued shares. The 2015 Plan provides that the exercise price of incentive stock options cannot be less than 100% of the fair market value of the common stock on the date of the award for participants who own less than 10% of the total combined voting power of stock, and not less than 110% for participants who own more than 10% of the voting power. Options and restricted stock granted under the 2015 Plan will vest over periods as determined by our Compensation Committee and approved by our Board of Directors.

We estimate the fair value of our stock-based awards to employees and non-employees using the Black-Scholes option-pricing model, which requires the input of highly subjective assumptions, including (a) the expected volatility of our stock, (b) the expected term of the award, (c) the risk-free interest rate, and (d) expected dividends. Due to the lack of a public market for the trading of our common stock and a lack of company-specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of companies in the pharmaceutical and biotechnology

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industries in a similar stage of development as us and that are publicly traded. For these analyses, we have selected companies with comparable characteristics to ours including enterprise value, risk profiles and with historical share price information sufficient to meet the expected life of the stock-based awards. We compute the historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of our stock-based awards. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available. We have estimated the expected life of our employee stock options using the "simplified" method, whereby, the expected life equals the average of the vesting term and the original contractual term of the option. The risk-free interest rates for periods within the expected life of the option are based on the U.S. Treasury yield curve in effect during the period the options were granted.

We are also required to estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from estimates. We use historical data to estimate pre-vesting option forfeitures and record stock-based compensation expense only for those awards that are expected to vest. To the extent that actual forfeitures differ from our estimates, the difference is recorded as a cumulative adjustment in the period the estimates were revised. Stock-based compensation expense recognized in the financial statements is based on awards that are ultimately expected to vest. Upon adopting ASU 2016-09 on January 1, 2017, we have elected to account for forfeitures as they occur.

Stock compensation expense incurred under the 2015 Plan was \$192 and \$993 during the year ended December 31, 2015 and 2016, respectively, consisting of stock-based compensation expense for awards granted to employees and our directors of \$39 and \$277 and non-employees and employees of the Relamorelin Company that are allocated to us of \$153 and \$716, respectively.

Stock compensation expense incurred under the 2015 Plan was \$473 and \$627 during the six months ended June 30, 2016 and 2017, respectively, consisting of stock-based compensation expense for awards granted to employees and our directors of \$100 and \$581, respectively, and non-employees and, for the six months ended June 30, 2016, employees of the Relamorelin Company that are allocated to us of \$373 and \$46, respectively. At June 30, 2017, we have unrecognized compensation expense related to these awards of \$3,622 and we expect to recognize our portion over a weighted-average period of approximately 2.65 years.

The following table summarizes the classification of our stock-based compensation expenses related to the 2015 Plan recognized in our statements of operations and comprehensive loss.

	Year Ended December 31,		Six Months Ended June 30,	
	2015	2016	2016	2017
Research and development	\$ 68	\$ 343	\$ 152	\$ 190
General and administrative	124	650	321	437
Total	<u>\$ 192</u>	<u>\$ 993</u>	<u>\$ 473</u>	<u>\$ 627</u>

The LLC entity applies the fair value recognition provisions of Financial Accounting Standards Board, or FASB, ASC Topic 718, *Compensation—Stock Compensation*, or ASC 718, to account for stock-based compensation. The LLC entity recognizes stock-based compensation expense based on the estimated fair value of each stock option or restricted common unit on the date of grant, net of estimated forfeitures. The grant date fair value of awards subject to service-based vesting, net of estimated forfeitures, is recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective awards. In accordance with ASC 718, stock-based compensation expense related to restricted common units that are subject to both performance and service-based vesting conditions is recognized using an accelerated recognition model.

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The fair value of a restricted common unit is estimated based on its fair value on the measurement date as if the restricted common unit was fully vested at that date, which is equivalent to the fair value of a common unit. Refer to our later discussion on the determination of the fair value of a common unit.

In addition to the assumptions used in the estimate of fair value of the LLC entity's restricted common units, the amount of compensation expense we and the LLC entity recognize in our statements of operations includes an estimate of restricted common unit forfeitures. Under ASC 718, we and the LLC entity are required to estimate the level of forfeitures expected to occur and record compensation expense only for those awards that we and the LLC entity ultimately expect will vest. Due to the lack of historical forfeiture activity, we and the LLC entity estimate our forfeiture rate based on data from a representative group of companies. Changes in the estimated forfeiture rate can have a significant impact on our stock-based compensation expense as the cumulative effect of adjusting the rate is recognized in the period the forfeiture estimate is changed. For example, if a revised forfeiture rate is higher than the previously estimated forfeiture rate, an adjustment is made that will result in a decrease to the stock-based compensation expense recognized in the financial statements. If a revised forfeiture rate is lower than the previously estimated forfeiture rate, an adjustment is made that will result in an increase to the stock-based compensation expense recognized in the financial statements. To date actual forfeitures have not been material.

The stock compensation expense allocated to us from the LLC entity was \$106 and \$175 for the years ended December 31, 2015 and 2016, respectively, and \$86 and \$71 for the six months ended June 30, 2016 and 2017, respectively. At June 30, 2017, we have unrecognized compensation expense related to the unvested portion of these awards of \$242 and we expect to recognize this amount over a weighted-average period of approximately 1.31 years.

The following table summarizes the classification of the LLC stock-based compensation expense recognized in our statements of operations and comprehensive loss.

	Year Ended December 31,		Six Months Ended June 30,	
	2015	2016	2016	2017
	(in thousands)			
Research and development	\$ 76	\$ 163	\$ 78	\$ 71
General and administrative	30	12	8	—
Total	<u>\$ 106</u>	<u>\$ 175</u>	<u>\$ 86</u>	<u>\$ 71</u>

Determination of the fair value of LLC common units and Rhythm Pharmaceuticals, Inc. common stock

We and the LLC entity operate as private companies with no active public market for our common stock and the LLC entity's common and preferred units. Therefore, the boards of directors estimated the fair value of our common stock and the LLC entity's common units at various dates, with input from management, considering our and the LLC entity's most recently available third-party valuations of common stock and common units, respectively, and the assessment of additional objective and subjective factors that were believed to be relevant and which may have changed from the date of the most recent valuation through the date of the applicable grant or award.

We and the LLC entity determined the estimated per share fair value of our common stock and the LLC entity's common units at various dates using contemporaneous valuations performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, or the Practice Aid, for financial reporting purposes.

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In conducting the contemporaneous valuations, we and the LLC entity considered all objective and subjective factors that we and the LLC entity believed to be relevant for each valuation conducted, including each respective entity's best estimate of its business condition, prospects and operating performance at each valuation date. Within the contemporaneous valuations performed, a range of factors, assumptions and methodologies were used.

The significant factors included:

- the lack of an active public market for our common stock and the LLC entity's common and preferred units;
- the prices at which we and the LLC entity sold our and its preferred shares and units, respectively, to outside investors in arm's length transactions, and the rights, preferences and privileges of those preferred shares and units, respectively, relative to common shares and units;
- our and LLC entity's results of operations, financial position and the status of each entity's research, and preclinical development efforts;
- the material risks related to each entity's business;
- the market performance of publicly traded companies in the life sciences and biotechnology sectors, and recently completed mergers and acquisitions of companies comparable to each entity;
- the likelihood of achieving a liquidity event for the holders of our common stock and the LLC entity's units, such as an initial public offering or sale of the company given prevailing market conditions; and
- any recent contemporaneous valuations of our common stock and the LLC entity's common units prepared in accordance with methodologies outlined in the Practice Aid.

Valuation methodologies

Our and the LLC entity's valuations of common stock and common units, respectively, were prepared utilizing the discounted cash flow, or DCF, method, the guideline public company, or GPC, method, the option-pricing method, or OPM, the probability-weighted expected return method, or PWERM, and a hybrid of the PWERM and OPM, which we refer to as the hybrid method:

- *Discounted Cash Flow Method.* Under the DCF method, projected cash flows are converted to present value by applying a discount rate based on an estimated cost of equity or an estimated cost of debt. The cost of equity is estimated based on rates of return required by outside investors. An estimated cost of debt is applied when future cash flows are adjusted for the probability of success in clinical trials.
- *Guideline Public Company Method.* Under the GPC method, our future value in an initial public offering is estimated based on a comparison to clinical-stage companies which have completed initial public offerings.
- *Option Pricing Method.* Under the OPM, common and preferred stock and common and preferred units are valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. Under this method, common stock and common units only have value if the funds available for distribution to common stock or common unit holders exceed the value of the liquidation preferences at the time of a liquidity event, such as a strategic sale or merger. Under the OPM, the value of one security, such as preferred stock or preferred units, is used to determine the value of the equity and the corresponding value of the common stock or common units.
- *Probability-Weighted Expected Return Method.* The PWERM is a scenario-based analysis that estimates the value per share based on the probability-weighted present value of expected future

investment returns, considering each of the possible outcomes available to each entity, as well as the economic and control rights of each equity class.

- *Hybrid Method.* The hybrid method is a PWERM where the equity value in one of the scenarios is calculated using the OPM. In the hybrid method used by each entity, three types of future-event scenarios were considered: an initial public offering, a sale and dissolution. Each entity used the OPM to allocate equity value for the unspecified liquidity event.
 - The enterprise value for the initial public offering and sale scenarios was determined using a market approach. Under the market approach, each entity estimated enterprise value using the guideline public company method. The guideline public company method includes comparisons to publicly traded companies in the relevant industry that recently completed initial public offerings. For the sale scenarios, each entity estimated a premium to the initial public offering value. The enterprise values are discounted back to the valuation date at an appropriate risk-adjusted discount rate.
 - The enterprise value for the unspecified liquidity event was determined using the OPM.

Contemporaneous valuation of the LLC entity common units as of May 1, 2015.

The LLC entity performed a contemporaneous valuation of its common units on May 1, 2015 to coincide with its planned issuance of certain equity grants. The LLC entity estimated the value of its equity using the DCF method under the income approach. The LLC entity allocated equity value among its preferred and common units using the hybrid method. The hybrid method is a form of PWERM which uses the OPM for at least one scenario. The LLC entity considered two scenarios: the OPM and a second scenario in which Actavis plc exercises its option to acquire the Relamorelin Company.

Retrospective valuation of the LLC entity common units as of July 15, 2015.

The LLC entity performed a retrospective valuation of its common units as of July 15, 2015 to coincide with the amendment of the Ipsen warrant. The LLC entity estimated the value of the equity of the Relamorelin Company using the DCF method under the income approach. For Rhythm Pharmaceuticals, Inc., the LLC entity estimated the value of the equity using the OPM. The LLC entity allocated equity value on its preferred and common units using a hybrid method. The hybrid method for the LLC entity considered two scenarios: the OPM and a second scenario in which Actavis plc exercises its option to acquire the Relamorelin Company.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. common stock as of August 3, 2015.

We performed a contemporaneous valuation of our common stock as of August 3, 2015 to coincide with the first tranche closing of our series A preferred stock financing. We valued our equity and allocated equity value using a hybrid backsolve method. The backsolve calculation reconciled to the price of our series A preferred stock. The hybrid method considered initial public offering and OPM scenarios. We relied on the GPC method to estimate equity value in the initial public offering scenario. This valuation also included a contemporaneous valuation of the 2015 Series A Investor Right/Obligation and 2015 Series A Investor Option to invest in the second tranche of our series A preferred stock financing. We valued the Series A Investor Right/Obligation as the probability-weighted present value of the future benefit associated with the second tranche investment. We valued the Series A Investor Option using the Black-Scholes option model.

Contemporaneous valuation of LLC entity common units as of September 30, 2015.

The LLC entity performed a contemporaneous valuation of its common units as of September 30, 2015 to coincide with the quarterly revaluation of non-employee stock grants. The LLC entity estimated the value of the equity of the Relamorelin Company using the DCF method under the income approach.

For Rhythm Pharmaceuticals, Inc., the LLC entity estimated the value of the equity using the hybrid method. Two scenarios were considered: an initial public offering and an OPM. The LLC entity allocated equity value on its preferred and common units using the hybrid method. The LLC entity considered three scenarios in its hybrid method: a distribution of Rhythm Pharmaceuticals, Inc. common shares based on an initial public offering equity value for Rhythm Pharmaceuticals, Inc., a distribution of common shares based on an OPM equity value for Rhythm Pharmaceuticals, Inc., and a scenario in which Actavis plc exercises its option to acquire the Relamorelin Company. This valuation also included a contemporaneous valuation of the 2015 Series A Investor Right/Obligation and 2015 Series A Investor Option to invest in the second tranche of our series A preferred stock financing. We valued the forward contract as the probability-weighted present value of the future benefit associated with the second tranche investment. We valued the option to invest in the second tranche using the Black-Scholes option model.

Contemporaneous valuation of LLC entity common units as of October 31, 2015.

The LLC entity performed a contemporaneous valuation of its common units as of October 31, 2015 to coincide with its planned issuance of certain equity grants. The LLC entity estimated the value of the equity of the Relamorelin Company using the DCF method under the income approach. For Rhythm Pharmaceuticals, Inc., the LLC entity estimated the value of the equity using the hybrid method. Two scenarios were considered: an initial public offering and an OPM. The LLC entity allocated equity value on its preferred and common units assuming separate distributions for Rhythm Pharmaceuticals, Inc. and the Relamorelin Company. For Rhythm Pharmaceuticals, Inc., the LLC entity considered a hybrid method with two scenarios: a distribution of Rhythm Pharmaceuticals, Inc. common shares based on an initial public offering and a distribution of common shares based on an OPM equity value. For the Relamorelin Company, the LLC entity allocated equity value based on the probability-weighted present value of an exercise by Actavis plc of its option to acquire the Relamorelin Company.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. common stock as of October 31, 2015.

We performed a contemporaneous valuation of our common stock as of October 31, 2015 to coincide with the planned issuance of certain equity grants. We valued our equity and allocated equity value using a hybrid backsolve method. The backsolve calculation reconciled to the price of our series A preferred stock. The hybrid method considered initial public offering and OPM scenarios. We relied on the GPC method to estimate equity value in the initial public offering scenario.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. Series A Investor Right/Obligation as of December 1, 2015.

We performed a contemporaneous valuation of the 2015 Series A Investor Right/Obligation to invest in the second tranche of our series A preferred stock financing. This valuation coincided with our 2015 Series A Second Tranche Closing on December 1, 2015. We valued the Series A Investor Right/Obligation as the benefit associated with the second tranche investment. The benefit is a function of the difference between the fair value of the Series A shares and the Series A Investor Right/Obligation exercise price on the date of closing and the number of shares acquired. We estimated the fair value of the Series A Investor Right/Obligation as the probability weighted average of two scenarios: an IPO and a remain-private scenario.

Contemporaneous valuation of LLC entity common units as of December 31, 2015.

The LLC entity performed a contemporaneous valuation of its common units as of December 31, 2015 to coincide with the quarterly revaluation of non-employee stock grants. The LLC entity estimated the value of the equity of the Relamorelin Company using the DCF method under the income approach. For Rhythm Pharmaceuticals, Inc., the LLC entity estimated the value of the equity using the hybrid method. Two scenarios were considered: an initial public offering and an OPM. The LLC entity allocated

equity value on its preferred and common units using the hybrid method. The LLC entity allocated equity value on its preferred and common units assuming separate distributions for Rhythm Pharmaceuticals, Inc. and the Relamorelin Company. For Rhythm Pharmaceuticals, Inc., the LLC entity considered a hybrid method with two scenarios: a distribution of Rhythm Pharmaceuticals, Inc. common shares based on an initial public offering and a distribution of common shares based on an OPM equity value. For the Relamorelin Company, the LLC entity allocated equity value based on the probability-weighted present value of an exercise by Actavis plc of its option to acquire the Relamorelin Company.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. common stock as of December 31, 2015.

We performed a contemporaneous valuation of our common stock as of December 31, 2015 to coincide with the issuance of certain equity grants. We valued our equity and allocated equity value using a hybrid backsolve method. The backsolve calculation reconciled to the price of our series A preferred stock. The hybrid method considered initial public offering and OPM scenarios. We relied on the GPC method to estimate equity value in the initial public offering scenario.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. common stock as of March 31, 2016.

We performed a contemporaneous valuation of our common stock as of March 31, 2016 to coincide with the issuance of certain equity grants. We valued our equity and allocated equity value using a hybrid backsolve method. The backsolve calculation reconciled to the price of our series A preferred stock. The hybrid method considered initial public offering and OPM scenarios. We relied on the GPC method to estimate equity value in the initial public offering scenario.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. common stock as of June 30, 2016.

We performed a contemporaneous valuation of our common stock as of June 30, 2016 to coincide with the issuance of certain equity grants. We valued our equity and allocated equity value using a hybrid backsolve method. The backsolve calculation reconciled to the price of our series A preferred stock. The hybrid method considered initial public offering and OPM scenarios. We relied on the GPC method to estimate equity value in the initial public offering scenario.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. common stock as of September 30, 2016.

We performed a contemporaneous valuation of our common stock as of September 30, 2016 to coincide with the issuance of certain equity grants. We valued our equity and allocated equity value using a hybrid backsolve method. The backsolve calculation reconciled to the price of our series A preferred stock. The hybrid method considered initial public offering and OPM scenarios. We relied on the GPC method to estimate equity value in the initial public offering scenario.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. common stock as of November 16, 2016.

We performed a contemporaneous valuation of our common stock as of November 16, 2016 to coincide with the revaluation of non-employee stock grants. As of November 16, 2016, the employees of the Relamorelin Company terminated their employment contracts with the Relamorelin Company and entered into new employment agreements with the Company. A new fair value of the remaining unvested awards for these employees was determined as of November 16, 2016 and will be expensed in accordance with ASC 718, Compensation—Stock Compensation over their remaining vesting period. We valued our equity and allocated equity value using a hybrid backsolve method. The backsolve calculation reconciled to the price of our series A preferred stock. The hybrid method considered initial public offering and OPM scenarios. We relied on the GPC method to estimate equity value in the initial public offering scenario.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. common stock as of December 31, 2016.

We performed a contemporaneous valuation of our common stock as of December 31, 2016 to coincide with the issuance of certain equity grants. We valued our equity and allocated equity value using a hybrid backsolve method. The backsolve calculation reconciled to the price of our series A preferred stock. The hybrid method considered initial public offering and OPM scenarios. We relied on the GPC method to estimate equity value in the initial public offering scenario. This valuation also included a contemporaneous valuation of the 2017 Series A Investor Instrument. The fair value of the 2017 Series A Investor Instrument is determined to be the sum of the fair values of the 2017 Series A Investor Right/Obligation and 2017 Series A Call Option. We valued the 2017 Series A Investor Right/Obligation as the probability-weighted present value of the future benefit associated with the second tranche investment. We valued the 2017 Investor Call Option using the Black-Scholes option model.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. common stock as of March 31, 2017.

We performed a contemporaneous valuation of our common stock as of March 31, 2017 to coincide with the issuance of certain equity grants. We valued our equity and allocated equity value using a hybrid backsolve method. The backsolve calculation reconciled to the price of our series A preferred stock. The hybrid method considered initial public offering and OPM scenarios. We relied on the GPC method to estimate equity value in the initial public offering scenario. This valuation also included a contemporaneous valuation of the 2017 Series A Investor Instrument. The fair value of the 2017 Series A Investor Instrument is determined to be the sum of the fair values of the 2017 Series A Investor Right/Obligation and 2017 Series A Call Option. We valued the 2017 Series A Investor Right/Obligation as the probability-weighted present value of the future benefit associated with the second tranche investment. We valued the 2017 Investor Call Option using the Black-Scholes option model.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. common stock as of June 30, 2017.

We performed a contemporaneous valuation of our common stock as of June 30, 2017 to coincide with the issuance of certain equity grants. We valued our equity and allocated equity value using a hybrid method. The hybrid method considered an initial public offering and a remain-private scenario in which value is allocated using the OPM. We relied on the GPC method to estimate equity value in the initial public offering scenario. In the remain-private scenario, equity value was estimated using an OPM backsolve calculation. This valuation also included a contemporaneous valuation of the 2017 Series A Investor Instrument. The fair value of the 2017 Series A Investor Instrument is determined to be the sum of the fair values of the 2017 Series A Investor Right/Obligation and 2017 Series A Call Option. We valued the 2017 Series A Investor Right/Obligation as the probability-weighted present value of the future benefit associated with the second tranche investment. We valued the 2017 Investor Call Option using the Black-Scholes option model.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. common stock as of August 31, 2017.

We performed a contemporaneous valuation of our common stock as of August 31, 2017 to coincide with the issuance of certain equity grants. We valued our equity and allocated equity value using a hybrid method. The hybrid method considered an initial public offering and a remain-private scenario in which value is allocated using the OPM. We relied on the GPC method to estimate equity value in the initial public offering scenario. In the remain-private scenario, equity value was estimated using an OPM backsolve calculation. This valuation also included a contemporaneous valuation of the 2017 Series A Investor Instrument as of August 17, 2017. The fair value of the 2017 Series A Investor Instrument is determined to be the sum of the fair values of the 2017 Series A Investor Right/Obligation and 2017 Series A Call Option. We valued the 2017 Series A Investor Right/Obligation as the probability-weighted present value of the future benefit associated with the second tranche investment. We valued the 2017 Investor Call Option using the Black-Scholes option model.

Results of Operations

Comparison of six months ended June 30, 2016 and June 30, 2017.

The following table summarizes our results of operations for the six months ended June 30, 2016 and 2017, together with the changes in those items in dollars and as a percentage:

	Six Months Ended June 30,		Change	
	2016	2017	\$	%
(in thousands)				
Statement of Operations Data:				
Operating Expenses:				
Research and development	\$ 8,544	\$ 10,270	\$ 1,726	20%
General and administrative	2,585	2,873	288	11%
Total operating expenses	11,129	13,143	2,014	18%
Loss from operations	(11,129)	(13,143)	(2,014)	(18)%
Other (expense) income, net	14	(19)	(33)	(236)%
Net loss and comprehensive loss	\$ (11,115)	\$ (13,162)	\$ (2,047)	(18)%

Research and development expense. Research and development expense increased by \$1.7 million to \$10.3 million in 2017 from \$8.5 million in 2016, an increase of 20%. The increase was primarily due to the initiation of additional new clinical trials in 2017 and an increase in other development activities associated with setmelanotide. We hired additional personnel in the clinical operations department at the end of 2016 and early 2017.

General and administrative expense. General and administrative expense increased by \$0.3 million to \$2.9 million in 2017 from \$2.6 million in 2016, an increase of 11%. The increase was primarily due to stock compensation expense related to new option grants in 2017 and general office expenses due to the increase in headcount at end of 2016 and early 2017.

Comparison of years ended December 31, 2015 and December 31, 2016.

The following table summarizes our results of operations for the years ended December 31, 2015 and 2016, together with the changes in those items in dollars and as a percentage:

	Year Ended December 31,		Change	
	2015	2016	\$	%
(in thousands)				
Statement of Operations Data:				
Operating Expenses:				
Research and development	\$ 7,148	\$ 19,594	\$ 12,446	174%
General and administrative	3,425	6,311	2,886	84%
Total operating expenses	10,573	25,905	15,332	145%
Loss from operations	(10,573)	(25,905)	(15,332)	(145)%
Other income (loss)	(500)	33	533	(107)%
Net loss and comprehensive loss	\$ (11,073)	\$ (25,872)	\$ (14,799)	(134)%

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Research and development expense. Research and development expense increased by \$12.4 million to \$19.6 million in 2016 from \$7.1 million in 2015, an increase of 174%. The increase was primarily due to non-cash expenses in 2016 of \$0.5 million in stock compensation. Our research and development costs increased subsequent to the initial series A financing at the end of fiscal year 2015 due to the initiation of additional new clinical trials and additional development activities for setmelanotide and the hiring of additional personnel in the clinical operations department in the fourth quarter of 2015 and 2016, as well as an increase in the overall proportion of research and development expenses allocated to us in 2016.

General and administrative expense. General and administrative expense increased by \$2.9 million to \$6.3 million in 2016 from \$3.4 million in 2015, an increase of 84%. The increase in general and administrative expense was primarily attributable to the write down of capitalized deferred issuance cost of \$1.8 million in 2016. As well as an increase in the overall proportion of general and administrative expenses allocated to us in 2016.

Liquidity and Capital Resources

Through August 2015, we received capital contributions from the Predecessor Company, the Relamorelin Company and the LLC entity from time to time as needed. In August 2015, December 2015, January 2017 and August 2017, we received aggregate gross proceeds of \$81.0 million from the sale of our series A preferred stock. As of June 30, 2017, our existing cash and cash equivalents and short-term investments were approximately \$17.7 million. After giving effect, on a pro forma basis, to the aggregate proceeds of the sale of our series A preferred stock in August 2017 of \$20.5 million, our cash and cash equivalents and short-term investments are \$38.2 million as of June 30, 2017.

Cash flows

The following table provides information regarding our cash flows for the years ended December 31, 2015 and 2016, and the six months ended June 30, 2016 and 2017:

	Year Ended December 31,			Six Months Ended June 30,		
	2015	2016	Change	2016	2017	Change
Net cash provided by (used in):						
Operating activities	\$ (6,977)	\$ (23,219)	\$ (16,242)	\$ (12,597)	\$ (13,158)	\$ (561)
Investing activities	(17)	(5,110)	(5,093)	(6,286)	(5,036)	1,250
Financing activities	41,711	—	(41,711)	—	20,377	20,377
Net increase (decrease) in cash and cash equivalents	<u>\$ 34,717</u>	<u>\$ (28,329)</u>	<u>\$ (63,046)</u>	<u>\$ (18,883)</u>	<u>2,183</u>	<u>21,066</u>

Net cash used in operating activities

The use of cash in all periods resulted primarily from our net losses adjusted for non-cash charges and changes in components of working capital.

Net cash used in operating activities was \$7.0 million for the year ended December 31, 2015, and consisted primarily of a net loss of \$9.4 million adjusted for non-cash items, which were comprised of stock-based compensation, warrant amendment expense and mark to market revaluation of the 2015 Series A Investor Right/Obligation. The significant items in the change in operating assets and liabilities include an increase in accounts payable, accrued expenses and other current liabilities of \$4.7 million offset by an increase of approximately \$2.1 million in deferred issuance costs and prepaid expenses and other current assets.

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Net cash used in operating activities was \$23.2 million for the year ended December 31, 2016, and consisted primarily of a net loss of \$24.5 million adjusted for non-cash items, which consisted of stock-based compensation, depreciation and amortization and deferred rent expense. The significant items in the change in operating assets and liabilities include a decrease in intercompany payable, accrued expense and deferred income of \$1.0 million, offset by an increase in accounts payables of approximately \$0.5 million and decreases in deferred issuance costs of approximately \$1.5 million.

Net cash used in operating activities was \$12.6 million for the six months ended June 30, 2016, and consisted primarily of a net loss of \$10.5 million adjusted for non-cash items, which consisted of stock-based compensation, depreciation and amortization and deferred rent expense. The significant items in the change in operating assets and liabilities include a decrease in accrued expenses of \$1.8 million and an increase in deferred issuance costs of approximately \$0.3 million.

Net cash used in operating activities was \$13.2 million for the six months ended June 30, 2017, and consisted primarily of a net loss of \$12.3 million adjusted for non-cash items, which consisted of stock-based compensation, depreciation and amortization and deferred rent expense and the mark to market revaluation of the Series A Investor Instrument. The change in operating assets and liabilities reflected a total use of cash of approximately \$0.8 million mainly with deferred issuance costs and accounts payables.

Net cash used in investing activities

Net cash used in investing activities for the year ended December 31, 2015 represent our design costs incurred related to our new facility lease.

Net cash used in investing activities for the year ended December 31, 2016 relates to the net purchases of short-term investments of \$4.1 million and the buildout of our new headquarters facility and furniture and equipment of \$1.1 million.

Net cash used in investing activities for the six months ended June 30, 2016 relates to the net purchases of short-term investments of \$5.3 million and the buildout of our new headquarters facility and furniture and equipment of \$1.0 million.

Net cash used in investing activities for the six months ended June 30, 2017 relates to the net purchases of short-term investments of \$5.0 million.

Net cash provided by financing activities

Net cash provided by financing activities in prior periods consisted primarily of capital contributions from the LLC entity in the form of cash transfers, and shared costs incurred by the Relamorelin Company and the Predecessor Company or paid by the Relamorelin Company or the Predecessor Company on our behalf.

Net cash provided by financing activities was \$41.7 million for the year ended December 31, 2015, consisting of \$39.6 million of net proceeds from the issuance of series A preferred stock and an equity contribution of \$2.1 million.

Net cash provided by financing activities was \$20.4 million for the six months ended June 30, 2017, and represents the net proceeds from the first tranche of our January 2017 issuance of series A preferred stock.

Funding requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the clinical development of and seek marketing approval for setmelanotide. In addition, if we obtain marketing approval for setmelanotide, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing and distribution are not the responsibility of potential collaborators. We expect to incur additional costs

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associated with operating as an independent company, and upon the closing of this offering, operating as a public company.

We expect that the net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses into the first half of 2019. We may need to obtain substantial additional funding in connection with our research and development activities and any continuing operations thereafter. If we are unable to raise capital when needed or on favorable terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of clinical trials for our setmelanotide program;
- the costs, timing and outcome of regulatory review of our setmelanotide program;
- the obligations owed to Ipsen pursuant to our license agreement;
- the extent to which we acquire or in-license other product candidates and technologies;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims; and
- our ability to establish and maintain additional collaborations on favorable terms, if at all.

Developing our setmelanotide program is a time-consuming, expensive and uncertain process that may take years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, setmelanotide, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of setmelanotide that we do not expect to be commercially available for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. In August 2015, December 2015, January 2017 and August 2017, respectively, we issued 25,000,000, 15,000,000, 20,475,001 and 20,474,998, shares of series A preferred stock, respectively, at a price of \$1.00 per share, resulting in gross proceeds of \$81.0 million.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, involves agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise funds through additional collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our setmelanotide program on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market our setmelanotide program that we would otherwise prefer to develop and market ourselves.

Our independent auditors have indicated in their report on our December 31, 2016 financial statements that there is substantial doubt about our ability to continue as a going concern. A "going concern" opinion indicates that the financial statements have been prepared assuming we will continue as a going concern and do not include adjustments to reflect the possible future effects on the recoverability

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and the classification of assets or the amounts and classification of liabilities that may result if we do not continue as a going concern.

Contractual obligations

We enter into agreements in the normal course of business with CROs and CMOs for clinical trials and clinical supply manufacturing and with vendors for clinical research studies and other services and products for operating purposes. We do not classify these as contractual obligations where the contracts are cancelable at any time by us, generally upon 30 days' prior written notice to the vendor.

Milestone and royalty payments associated with our license agreements with Ipsen and Camurus have not been included as contractual obligations as we cannot reasonably estimate if or when they will occur. Under the terms of the Ipsen license agreement, assuming that setmelanotide is successfully developed, receives regulatory approval and is commercialized, Ipsen may receive aggregate payments of up to \$40.0 million upon the achievement of certain development and commercial milestones under the license agreement and royalties on future product sales. The majority of the aggregate payments under the Ipsen license agreement are for milestones that may be achieved no earlier than first commercial sale of setmelanotide. In the event that we enter into a sublicense agreement, we will make payments to Ipsen, depending on the date of the sublicense agreement, ranging from 10% to 20% of all revenues actually received under the sublicense agreement. Under the terms of the Camurus license agreement, assuming that setmelanotide is successfully developed, receives regulatory approval and is commercialized, Camurus may receive aggregate payments of up to \$64.75 million upon the achievement of certain development and commercial milestones under the license agreement and royalties on future product sales. The majority of the aggregate payments under the Camurus license agreement are for milestones that may be achieved no earlier than first commercial sale of setmelanotide.

In November 2015, we entered into a Lease Agreement for an office facility at 500 Boylston Street, Boston, Massachusetts. The lease term commenced in May 2016 and has a term of five years with a five year renewal option to extend the lease.

Future minimum payments under the operating lease agreements as of December 31, 2016, are as follows:

	<u>Operating Lease</u>
2017	\$ 291
2018	298
2019	305
2020	311
2021	131
Total	1,336

Off-balance Sheet Arrangements

We did not have, during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable SEC rules.

Quantitative and Qualitative Disclosures about Market Risk

We are not exposed to market risk related to changes in interest rates or foreign currency exchange rates.

JOBs Act

In April 2012, the JOBS Act was enacted. Section 107 of the JOBS Act provides that an "emerging growth company," or EGC, can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. Thus, an EGC can delay the adoption of certain newly implemented accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

We are in the process of evaluating the benefits of relying on other exemptions and reduced reporting requirements under the JOBS Act. Subject to certain conditions, as an EGC, we intend to rely on certain of these exemptions, including without limitation, (i) providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and (ii) complying with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis. We will remain an EGC until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of this offering, (b) in which we have total annual gross revenue of at least \$1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior December 31st, and (2) the date on which we have issued more than \$1.0 billion in non-convertible debt securities during the prior three-year period.

BUSINESS**Overview**

We are a biopharmaceutical company focused on the development and commercialization of peptide therapeutics for the treatment of rare genetic deficiencies that result in life-threatening metabolic disorders. Our lead peptide product candidate is setmelanotide, a potent, first-in-class melanocortin-4 receptor, or MC4R, agonist for the treatment of rare genetic disorders of obesity. We believe setmelanotide, for which we have exclusive worldwide rights, has the potential to serve as replacement therapy for the treatment of melanocortin-4, or MC4, pathway deficiencies. MC4 pathway deficiencies result in the disruption of satiety signals and energy homeostasis in the body, which, in turn, leads to intense feelings of hunger and to obesity. Our development efforts are initially focused on obesity related to six single gene-related, or monogenic, MC4 pathway deficiencies—pro-opiomelanocortin, or POMC, leptin receptor, or LepR, Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous, and POMC epigenetic disorders—for which there are currently no effective or approved treatments. We believe that the MC4 pathway is a compelling target for treating these genetic disorders because of its critical role in regulating appetite and weight by promoting satiety and weight control, and that peptide therapeutics are uniquely suited for activating this target.

We have demonstrated proof of concept in Phase 2 clinical trials in POMC deficiency obesity, LepR deficiency obesity, and Bardet-Biedl syndrome, three genetic disorders of extreme and unrelenting appetite and obesity, in which setmelanotide dramatically reduced both weight and hunger. The U.S. Food and Drug Administration, or FDA, has acknowledged the importance of these results by giving setmelanotide breakthrough therapy designation for the treatment of obesity associated with genetic defects upstream of the MC4 receptor in the leptin-melanocortin pathway, which includes both POMC deficiency obesity and LepR deficiency obesity. Setmelanotide is currently in Phase 3 development for POMC deficiency obesity and LepR deficiency obesity. We are currently enrolling patients in our POMC deficiency obesity Phase 3 clinical trial. We expect to complete enrollment by the end of 2017 and to report Phase 3 data in the first half of 2019. We expect to enroll the first patient in our LepR deficiency obesity Phase 3 clinical trial in the second half of 2017, and to complete enrollment in 2018. We recently demonstrated preliminary proof of concept in our Phase 2 clinical trial in Bardet-Biedl syndrome, indicating that this is also a setmelanotide-responsive, upstream MC4 pathway disorder. We are continuing to enroll patients in this trial and expect to report preliminary Phase 2 results in the fourth quarter of 2017. We expect to initiate a Phase 3 clinical trial in Bardet-Biedl syndrome in 2018. We have also initiated Phase 2 clinical trials in Alström syndrome, POMC heterozygous deficiency obesity and POMC epigenetic disorders, and expect to enroll patients in these trials in the second half of 2017. We anticipate reporting preliminary results in these additional Phase 2 indications in the first half of 2018. Approximately 275 obese subjects and patients have been treated with setmelanotide in previous and ongoing clinical trials in which setmelanotide demonstrated statistically significant weight loss with good tolerability.

Obesity is epidemic in the United States and current treatment approaches have demonstrated limited long-term success for most obese patients. We are taking a different approach to obesity drug development by leveraging new understanding of the genetic causes of severe obesity to develop innovative therapies that we believe have the potential for compelling efficacy. Setmelanotide's unique mechanism of action at MC4R enables a targeted approach to treating very severe obesity in patients with specific, monogenic defects in the MC4 signaling pathway. By restoring impaired function in this pathway, setmelanotide can serve as replacement therapy for genetic deficiencies, with the potential for dramatic improvements in weight and appetite. We believe we are at the forefront of improving treatment outcomes in subtypes of severe obesity that are caused by genetically-defined defects in the MC4 pathway.

Setmelanotide activates MC4R, which is part of the key pathway that can independently regulate energy homeostasis, which refers to the body's energy balance, and appetite. The critical role of the MC4 pathway in weight regulation was validated with the discovery that single genetic defects along this pathway

result in early onset and severe obesity. An expanding set of severe obesity genetic defects are now identified that involve genes in the pathway which are either upstream of MC4R—for example POMC deficiency obesity and LepR deficiency obesity—or genes that are downstream of MC4R or affect MC4R itself. We are focusing setmelanotide clinical development on patients with monogenic upstream genetic defects in which obesity is life-threatening but the downstream MC4 pathway is fully functional. We believe setmelanotide has the potential to restore lost activity in the MC4 pathway by bypassing the defects upstream of MC4R, and activating the MC4 pathway below such defects. In this way, setmelanotide may serve as replacement therapy to reestablish weight and appetite control in patients with these genetic disorders.

The first generation of MC4R agonists were predominantly small molecules that failed in clinical trials due to safety issues, particularly increases in blood pressure, in addition to having limited efficacy. In contrast, setmelanotide, a novel eight amino acid peptide, retains the specificity and functionality of the naturally occurring hormone that activates MC4R, and has exhibited preliminary evidence of efficacy without adversely affecting blood pressure in our Phase 1 and ongoing Phase 2 clinical trials. We are currently evaluating setmelanotide, which is administered by subcutaneous, or SC, injection, for the treatment of six genetic disorders of obesity: POMC deficiency obesity, LepR deficiency obesity, Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders. We have positive Phase 2, proof of concept results for two of these indications thus far—POMC deficiency obesity and LepR deficiency obesity—and both indications are currently in Phase 3 development.

POMC deficiency obesity is a life-threatening, ultra-rare orphan disease, with approximately 50 patients reported to date. Ultra-rare orphan diseases are generally categorized as those that affect fewer than 20 patients per million. We estimate that our addressable patient population for this disorder is approximately 100 to 500 patients in the United States. Patients with POMC deficiency have unrelenting hunger, or hyperphagia, that begins in infancy and they develop severe, early onset obesity. POMC deficiency obesity results from two different homozygous genetic defects, both upstream of MC4R, that result in loss of function in the MC4 pathway. Currently, there is no approved treatment for the obesity and hyperphagia associated with this genetic disorder. We have initiated a Phase 3 open label, single arm, multinational trial to evaluate the safety and efficacy of setmelanotide for POMC deficiency obesity, with setmelanotide administered once daily by subcutaneous, or SC, injection for 12 months. We are currently enrolling patients in this POMC deficiency obesity Phase 3 clinical trial. We expect to complete enrollment by the end of 2017 and to report Phase 3 data in the first half of 2019. Previously, we completed a positive Phase 2 clinical trial in which two patients were enrolled and received treatment. The first patient in this trial lost 146.6 lbs over 118 weeks, from a baseline weight of 341.7 lbs, and the second patient lost 89.3 lbs over 64 weeks, from a baseline weight of 336.9 lbs. Both patients experienced substantial reductions in hunger, with hunger scores falling to one to two from baseline scores of nine to 10. Hunger scores were measured using a Likert score of zero to 10, where zero represents no hunger and 10 represents extreme hunger. Setmelanotide was generally well tolerated in this Phase 2 trial.

LepR deficiency obesity is an ultra-rare orphan disease that results in hyperphagia and severe early-onset obesity, with an estimated prevalence of 1% of subjects with severe, early-onset obesity. We estimate that our addressable patient population for this disorder is approximately 500 to 2,000 patients in the United States. Like other deficiencies upstream in the MC4 pathway, LepR deficiency results in loss of function in the MC4 pathway. Therefore, patients with this indication also manifest hyperphagia and severe obesity from early childhood. Currently, there is no approved treatment for the obesity and hyperphagia associated with LepR deficiency obesity. We have initiated a Phase 3 open label, single arm, multinational trial to evaluate the safety and efficacy of setmelanotide for LepR deficiency obesity, with setmelanotide administered once daily by SC injection for 12 months. We expect to enroll the first patient in our LepR deficiency obesity Phase 3 clinical trial in the second half of 2017, and to complete enrollment in 2018. Previously, we completed a positive Phase 2 clinical trial in which three patients were enrolled and

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received treatment in this trial each experiencing significant weight loss and substantial reductions in hunger. Setmelanotide was generally well tolerated in this Phase 2 trial.

Based on our POMC deficiency obesity and LepR deficiency obesity Phase 2 results, the FDA granted setmelanotide breakthrough therapy designation for the treatment of obesity associated with genetic defects upstream of the MC4 receptor in the leptin-melanocortin pathway, which includes both POMC deficiency obesity and LepR deficiency obesity, enabling an expedited path to approval of setmelanotide for these two indications. In April 2016, the FDA granted our orphan drug designation request for setmelanotide for the treatment of POMC deficiency obesity.

Bardet-Biedl syndrome is a life-threatening, ultra-rare orphan disease with a prevalence of approximately one in 100,000 in North America. We estimate that our addressable patient population for Bardet-Biedl syndrome obesity is approximately 1,500 to 2,500 patients in the United States. Bardet-Biedl syndrome is a monogenic disorder that causes severe obesity and hyperphagia as well as vision loss, polydactyly, kidney abnormalities, and other signs and symptoms. Currently there are no approved or effective therapies for Bardet-Biedl syndrome. We recently demonstrated preliminary proof of concept based on data from five patients in our Phase 2 clinical trial in Bardet-Biedl syndrome, indicating that this is also a setmelanotide-responsive, upstream MC4 pathway disorder. Four of these five patients showed early, but significant weight loss and all five patients showed clear improvements in every hunger assessment. We are continuing to enroll patients in this trial and expect to report preliminary Phase 2 results in the fourth quarter of 2017. Setmelanotide has so far been generally well tolerated in this trial. We expect to initiate a Phase 3 clinical trial in Bardet-Biedl syndrome in 2018.

We are also focusing on additional monogenic, upstream MC4 pathway deficiencies for which setmelanotide can function as replacement therapy and provide activation of the pathway downstream of the defect, promoting satiety and weight control. We have initiated a Phase 2 proof of concept trial for the treatment of Bardet-Biedl syndrome, which is a rare monogenic disorder that we believe has an addressable patient population of approximately 1,500 to 2,500 patients in the United States. Bardet-Biedl syndrome causes severe obesity and hyperphagia as well as vision loss, polydactyly, kidney abnormalities, and other signs and symptoms. For these patients, hyperphagia and obesity can have significant health consequences for which there is currently no approved treatment. We have initiated Phase 2 trials for Alström syndrome, a life-threatening, ultra-rare orphan disease, for which we estimate our addressable population is approximately 500 to 1,000 patients worldwide, for POMC heterozygous deficiency obesity, for which we estimate our addressable population is approximately 4,000 patients in the United States, and for POMC epigenetic disorders. For these patients, hyperphagia and obesity can have significant health consequences for which there is currently no approved treatment. We expect to enroll patients with Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders in the second half of 2017 and to report preliminary results from these trials in the first half of 2018.

Our company was founded in November 2008 by former biopharmaceutical executives who have successfully developed, commercialized and in-licensed innovative pharmaceutical products, and we have subsequently expanded our senior management team to further broaden our team's experience in developing, registering and commercializing new drugs. In addition, our scientific advisory board, or SAB, members have extensive clinical expertise in obesity, endocrinology and metabolic diseases. We intend to leverage the experience of our senior management team and SAB to develop and commercialize setmelanotide. Through our senior management team's network of industry contacts, we will continue to evaluate additional product candidate licensing and acquisition opportunities. We are backed by strong and dedicated investors that include both private equity venture capital funds and public healthcare investment funds. Our investors include MPM Capital, New Enterprise Associates, Third Rock Ventures, Ipsen, Pfizer Venture Investments, OrbiMed, Deerfield Management and two public healthcare investment funds.

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Our patent portfolio includes composition of matter patents for setmelanotide that expire in the United States in 2027, with possible patent term extension to 2032 under the Hatch-Waxman Act.

Our Strategy

Our goal is to be a leader in developing and commercializing targeted therapies for genetic deficiencies that result in life-threatening metabolic disorders. The key components of our strategy are:

- **Rapidly develop setmelanotide for rare genetic disorders of obesity caused by MC4 pathway deficiencies.** We are aiming to dramatically improve patient outcomes in severe obesity by targeting setmelanotide's mechanism of action to the treatment of patients with genetically-defined defects in the MC4 pathway. We are focusing setmelanotide clinical development on monogenic upstream genetic defects in which obesity is life-threatening but where the downstream MC4 pathway is fully functional. We intend to pursue faster paths to approval for setmelanotide in these orphan disorders. We believe that focusing on these rare life-threatening conditions enables us to rapidly develop and commercialize setmelanotide using relatively small clinical trials.
- **Advance setmelanotide for POMC deficiency obesity and LepR deficiency obesity as our first indications in upstream MC4 pathway deficiencies.** We are currently evaluating setmelanotide for the treatment of six genetic disorders of obesity: POMC deficiency obesity, LepR deficiency obesity, Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders. We currently have a Phase 3 trial underway for POMC deficiency obesity and expect to report Phase 3 data in the first half of 2019. We have also initiated a Phase 3 trial for LepR deficiency obesity. We expect to enroll the first patient in our LepR deficiency obesity Phase 3 clinical trial in the second half of 2017, and to complete enrollment in 2018. We are working with the FDA, based on our breakthrough therapy designation, to prepare NDA filings with an expedited path to approval for POMC deficiency obesity and LepR deficiency obesity.
- **Expand setmelanotide development to additional upstream MC4 pathway deficiencies, including Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders.** We believe we can leverage our mechanistic understanding of and experience with both POMC deficiency obesity and LepR deficiency obesity to advance development of setmelanotide for other upstream MC4 pathway deficiencies. Accordingly, we have initiated Phase 2 clinical trials in these rare genetic disorders. We have obtained preliminary proof of concept in Bardet-Biedl syndrome, demonstrating that this is also a setmelanotide-responsive, upstream MC4 pathway disorder. We expect to report preliminary Phase 2 results in Bardet-Biedl syndrome in the fourth quarter of 2017 and preliminary results for the other Phase 2 indications in the first half of 2018.
- **Commercialize setmelanotide for rare disease indications in core strategic markets.** We intend to establish our own commercial sales and marketing organization in the United States and other core strategic markets. We expect this sales organization will target physicians treating these rare genetic disorders of obesity, including pediatric and adult endocrinologists. We believe that building our own commercial operations will deliver a greater return on our product investment than if we license the rights to commercialize these products to third parties. We may also selectively establish partnerships in markets outside the United States for sales, marketing and distribution.
- **Leverage the broad experience of our team in clinical and commercial drug development, and product acquisitions.** We will apply our team's extensive experience in developing and commercializing innovative medicines to the development and launch of setmelanotide. In addition, we intend to identify and acquire new pipeline programs in related diseases. Our team is complemented by highly experienced external consultants and collaborators in the areas of drug discovery, development, manufacturing and regulatory approval.

Our Product Pipeline

The following chart depicts key information regarding the development of setmelanotide, including the indications we are pursuing within MC4 pathway deficiencies, the current state of development and our expected upcoming milestones:

Indication	Phase 1	Phase 2	Phase 3	Proof-of-Concept	Last Event	Next Expected Event
POMC Deficiency Obesity			Green arrow pointing right	✓	Positive Phase 2; Phase 3 initiated	Phase 3 results 1H 2019
Leptin Receptor Deficiency Obesity			Green arrow pointing right	✓	Positive Phase 2; Phase 3 initiated	Phase 3 enrollment complete 2018
Bardet-Biedl Syndrome			Green arrow pointing right	✓	Preliminary proof of concept demonstrated	Preliminary Phase 2 results 4Q17; initiate Phase 3 2018
POMC Heterozygous Deficiency Obesity			Green arrow pointing right		Initiated Phase 2	Phase 2 results 1H 2018
Alström Syndrome			Green arrow pointing right		Initiated Phase 2	Phase 2 results 1H 2018
POMC Epigenetic Disorders			Green arrow pointing right		Initiated Phase 2	Phase 2 results 1H 2018

Market Overview

Recent Advances in the Understanding of Obesity

Diet and lifestyle modifications remain the cornerstones of weight loss therapy, but they are limited by a lack of long-term success for most obese patients. The long-term efficacy of these interventions and for existing drug therapies is often limited by the counter-regulatory mechanisms of the human body. For example, with diet induced weight loss, typically there is a large decrease in energy expenditure that offsets that weight loss. Accordingly, the discovery that the MC4 pathway can regulate both appetite and energy homeostasis separately—helping maintain the balance between food intake and energy burn—has defined an important target for therapeutics. In addition to POMC deficiency obesity and LepR deficiency obesity, recent advances in genetic studies have identified several diseases that are the result of genetic defects affecting the MC4 pathway, including Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders. With a deeper understanding of this critical signaling pathway, we are taking a different approach to drug development by focusing on specific genetic deficiencies affecting the MC4 pathway. We believe that this approach has the potential to provide dramatic improvements in weight and appetite by restoring lost function in the MC4 pathway.

Obesity Caused by Rare Genetic Deficiencies Affecting the MC4 Pathway

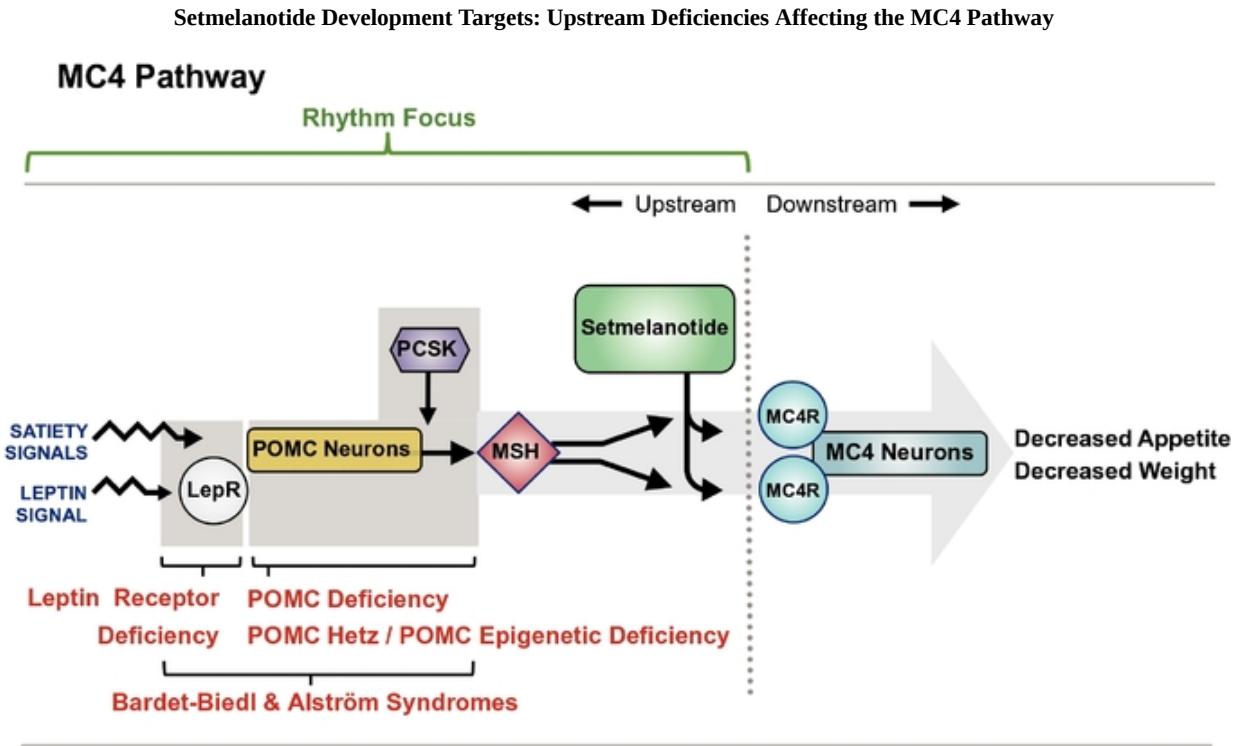
The MC4 pathway serves a critical role in the control of food intake and energy balance. Its activity decreases appetite and caloric intake, and increases energy expenditure, with MC4R acting as the final step in the signaling pathway. This important hypothalamic, or lower brainstem, pathway has been the focus of extensive investigation for many years, and we have a deep understanding of this mechanism, which is unlike the targets of most other anti-obesity therapies. As a result, we believe we can better predict the

efficacy and safety profile expected from modulating this target. The critical role of the MC4 pathway in weight regulation was also validated with the discovery that single genetic defects at many points in this pathway result in early onset, severe obesity.

The MC4 pathway is illustrated in the figure below, from the activation of the pathway to the resulting decrease in appetite and weight. Under normal conditions, POMC neurons are activated by brain satiety signals, including those resulting from the hormone leptin acting through LepR. POMC neurons produce a protein, which is specifically processed by the proprotein convertase subtilisin/kexin 1, or PCSK, enzyme, into melanocyte stimulating hormone, or MSH, the natural ligand, or activator, for MC4R. When genetic mutations disrupt this pathway, the result is hyperphagia and severe obesity.

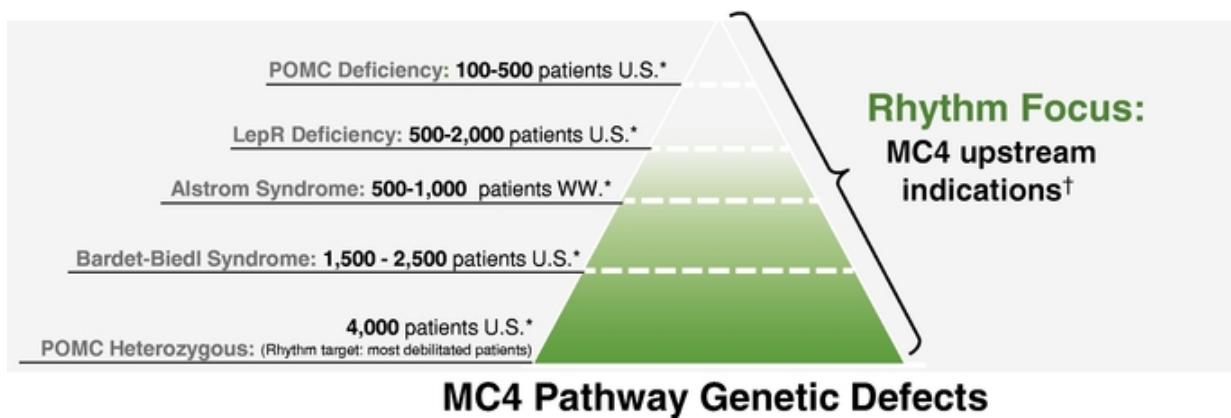
We are focused on developing setmelanotide for genetic disorders that result in defects in this pathway that are upstream of MC4R. Setmelanotide has the potential to restore lost function in this pathway by activating the intact MC4 pathway below the genetic defect. In this way, we believe setmelanotide acts as replacement therapy.

The figure below also illustrates some of the upstream MC4 pathway deficiencies that are the targets of our development activities.



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The figure below summarizes the indications on which we are focusing for the development of setmelanotide, including our estimates for the addressable patient populations within these indications.



* The patient numbers above are based on company estimates.

† Epidemiological estimates are not yet available for POMC epigenetic disorders.

We believe that the patient populations in the European Union are at least as large as those in the United States. However, we do not have comparable epidemiological data from the European Union and these estimates are therefore based solely on applying relative population percentages to the Company-derived estimates described above.

Obesity Caused by Upstream Genetic Deficiencies Affecting the MC4 Pathway

We have completed three positive Phase 2 trials of setmelanotide that provide proof of concept for three upstream MC4 pathway genetic defects in which obesity is life-threatening but the downstream MC4 pathway is fully functional: POMC deficiency obesity, LepR deficiency obesity, and Bardet-Biedl syndrome, which together we estimate have an addressable population of up to 5,000 people in the United States.

POMC Deficiency Obesity

POMC deficiency obesity is an ultra-rare genetic disorder, with severe, early onset obesity, defined here as a body mass index, or BMI, of greater than 40 kg/m², and hyperphagia as hallmark clinical features. Patients with POMC deficiency obesity are extremely rare. There are approximately 50 patients with POMC deficiency obesity noted in a series of published case reports, each mostly reporting a single or small number of patients. However, we estimate that our addressable patient population for this disorder is approximately 100 to 500 patients in the United States, as most of the reported cases are from a small number of academic research centers, and because genetic testing for POMC deficiency is often unavailable and rarely performed. Based on discussions with experts in rare diseases, we also believe the number of diagnosed cases will increase several-fold with increased awareness of this disorder and the availability of new treatments.

POMC deficiency obesity is caused by the loss of both genetic copies of either the gene for POMC or the gene for PCSK. This results either in loss of POMC neuropeptide synthesis, in the case of homozygous deficiency in the POMC gene, or in disruption of the required processing of the POMC neuropeptide product to MSH by the PCSK enzyme, in the case of homozygous deficiency in the PCSK gene. The end result of both of these two homozygous genetic defects is lack of MSH to bind and activate MC4R, ultimately leading to the lack of stimulation of downstream MC4 neurons and causing severe, early onset

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obesity and hyperphagia. POMC homozygous deficiency may also be associated with hormonal deficiencies, such as hypoadrenalinism, as well as red hair and fair skin.

POMC deficiency is characterized by voracious infant feeding, rapid weight gain and severe obesity, often in early infancy, with patients demonstrating remarkable weight increases many standard deviations from the normal weight growth curves. These patients and their caregivers have attempted to stabilize body weight with the help of psychologists, nutritionists and pediatric endocrinologists, all without significant success. We are currently enrolling patients in our POMC deficiency obesity Phase 3 clinical trial. We expect to complete enrollment by the end of 2017 and to report Phase 3 data in the first half of 2019. Currently there are no approved or effective therapies for POMC deficiency obesity.

Leptin Receptor Deficiency Obesity

LepR deficiency obesity is an ultra-rare genetic disorder that causes hyperphagia and severe, early onset obesity. LepR deficiency accounts for an estimated 1% of cases of severe, early onset obesity. Based on epidemiology studies in small cohorts of patients with severe, early onset obesity, we estimate that our addressable patient population for this disorder is approximately 500 to 2,000 patients in the United States.

Leptin's role in obesity has been elucidated by characterization of severely obese people with homozygous mutations that impair the activity of leptin, including disruption of signaling at the LepR, known as LepR deficiency obesity. Under normal conditions, leptin can activate POMC neurons and the downstream MC4, but like other deficiencies upstream in the MC4 pathway, lack of signaling at LepR results in loss of function in the MC4 pathway.

Like POMC deficiency obesity, patients with LepR deficiency obesity exhibit hyperphagia and severe obesity from early childhood. LepR deficiency is also associated with hypogonadism and reduced immune function. We expect to enroll the first patient in our LepR deficiency obesity Phase 3 clinical trial in the second half of 2017, and to complete enrollment in 2018. Currently there are no approved or effective therapies for LepR deficiency obesity.

Bardet-Biedl Syndrome

Bardet-Biedl syndrome is a life-threatening, ultra-rare orphan disease with a prevalence of approximately one in 100,000 in North America. We estimate that our addressable patient population for Bardet-Biedl syndrome obesity is approximately 1,500 to 2,500 patients in the United States. Bardet-Biedl syndrome is a monogenic disorder that causes severe obesity and hyperphagia as well as vision loss, polydactyly, kidney abnormalities, and other signs and symptoms. For Bardet-Biedl syndrome patients, hyperphagia and obesity can have significant health consequences.

Bardet-Biedl syndrome is part of a class of disorders called ciliopathies, or disorders associated with the impairment of cilia function in cells. Cilia are hair-like cellular projections that play a fundamental role in the regulation of several biological processes, including satiety signaling. Cilia dysfunction is thought to contribute to hyperphagia and obesity in Bardet-Biedl syndrome. Bardet-Biedl syndrome is a genetically heterogeneous disease that is caused by as many as 21 separate Bardet-Biedl loci defects that result in a similar syndrome, though each Bardet-Biedl syndrome patient only has one of these defects.

Recent scientific studies identify deficiencies affecting the MC4 pathway as a potential cause of the obesity and hyperphagia associated with Bardet-Biedl syndrome and demonstrate that an MC4R agonist can directly impact these symptoms. Studies in mouse models of Bardet-Biedl syndrome show that deficiencies in the MC4 pathway contribute to the obesity and hyperphagia in Bardet-Biedl syndrome, with animals developing hyperphagic tendencies as early as 10 weeks of age. Notably, these mice have decreased leptin receptor signaling, with the essential hallmarks of failure to activate POMC neurons. The potential utility of MC4 agonists is also supported by studies in Bardet-Biedl syndrome rodent models, where mice have responded to an MC4 agonist resulting in reduced food intake and body weight. We have obtained preliminary proof of concept in Bardet-Biedl syndrome demonstrating that this is also a setmelanotide-responsive, upstream MC4 pathway disorder. We anticipate reporting preliminary results for Bardet-Biedl syndrome in the fourth quarter of 2017, and initiating Phase 3 clinical trials in 2018. Currently there are no approved or effective therapies for Bardet-Biedl syndrome.

Other Upstream Genetic Defects in the MC4 Pathway

In addition to POMC deficiency obesity, LepR deficiency obesity and Bardet-Biedl syndrome, there are other upstream, MC4 pathway deficiencies for which we believe setmelanotide may function as replacement therapy, including defects that partially modulate POMC activity, such as POMC heterozygous deficiency obesity and POMC epigenetic disorders, as well as deficiencies that may indirectly impair POMC and LepR signaling, such as Alström syndrome.

Alström Syndrome

Alström syndrome is a life-threatening, ultra-rare orphan disease with a prevalence of approximately one in 1,000,000 in North America. We estimate that our addressable patient population for Alström syndrome is approximately 500 to 1,000 patients worldwide. Alström syndrome is a monogenic disorder that causes childhood obesity and hyperphagia as well as progressive vision loss, deafness, cardiomegaly, insulin resistance and other signs and symptoms. Variable features include short stature, cardiomyopathy, and progressive lung, liver, and kidney dysfunction. Symptoms of Alström syndrome first appear in infancy, and progressive development of multi-organ pathology leads to a reduced life expectancy, with survival rare beyond the age of 50.

Alström syndrome is a ciliopathy caused by mutations in the ALMS1 gene, which has been shown to be important for cilia function. Like Bardet-Biedl syndrome, recent scientific studies identify genetic deficiencies affecting the MC4 signaling pathway as a potential cause of the obesity and hyperphagia associated with Alström syndrome. Studies in a mouse model of Alström syndrome show a reduction in the number of cilia in specific neurons in the hypothalamus that are critical for MC4 pathway signaling. While Alström syndrome is less well studied than Bardet-Biedl syndrome, the similar pathophysiology of ciliary dysfunction and clinical presentation support that deficiencies in the MC4 pathway are implicated in the obesity and hyperphagia observed in Alström syndrome. We expect to enroll patients with Alström syndrome in a Phase 2 clinical trial in the second half of 2017 and anticipate reporting preliminary results in the first half of 2018. Currently there are no approved or effective therapies for Alström syndrome.

POMC Heterozygous Deficiency Obesity

POMC heterozygous deficiency results in a strong predisposition to obesity, though the epidemiology and clinical characterization of these patients is less well known. POMC heterozygous deficiency obesity is caused by the loss of one of the two genetic copies of either the gene for POMC or the gene for PCSK. An estimated 2% of severe, early onset obesity patients have POMC heterozygous deficiency obesity, which is much more common than the ultra-rare POMC deficiency obesity in which both copies of either the POMC or PCSK genes are impaired. We believe that the most severe POMC heterozygous deficiency obesity patients may be suitable for treatment with setmelanotide. We estimate that our addressable patient population within severe POMC heterozygous deficiency obesity is approximately 4,000 patients in the United States, based on epidemiology studies in small cohorts of patients with severe early onset obesity and adult obesity. Animal models support that such heterozygous deficiency in the critical MC4 pathway can result in a strong predisposition to severe obesity. The effect of heterozygous deficiency was first demonstrated in MC4R heterozygous deficiency obesity.

It is thought that the obesity of patients with POMC heterozygous deficiency may have a broader spectrum of severity than POMC deficiency obesity. Therefore, our focus will be on the most severe of the POMC heterozygous deficiency obesity patients, with our estimate that only a small percentage of these patients will benefit from targeted therapy with substantial efficacy. As a result, we have initiated a Phase 2 proof of concept trial to confirm our hypothesis that the subset of patients with very severe POMC heterozygous deficiency obesity may be highly responsive to setmelanotide therapy. We expect to enroll patients with POMC heterozygous deficiency obesity in a Phase 2 clinical trial in the second half of 2017 and to report preliminary results in the first half of 2018. There are currently no approved or effective therapies for POMC heterozygous deficiency obesity.

POMC Epigenetic Disorders

Recent scientific studies have identified patients with obesity due to a partial lack of MSH that is caused by epigenetic POMC variant. Given the recent discovery of these epigenetic disorders, there is currently no epidemiology data that defines the prevalence of POMC epigenetic disorders. However, we believe these are rare disorders. Epigenetics implies DNA modifications, which can change gene expression without altering the DNA sequence itself. The most stable epigenetic modification is called DNA methylation. Recently, our academic collaborators in Berlin have described a POMC hypermethylation variant, which correlates with increased body weight in children and adults. Therefore, the presence of the POMC epigenetic variant leads to an increased risk of obesity based on reduced POMC gene activity. We expect that these patients under-express the POMC gene product and as a result have a partial MSH deficiency. We have initiated a Phase 2 proof of concept trial to confirm our hypothesis that the subset of patients with very severe POMC epigenetic disorders may be highly responsive to setmelanotide therapy. We expect to enroll patients with POMC epigenetic disorders in a Phase 2 clinical trial in the second half of 2017 and anticipate reporting preliminary results in the first half of 2018. There are currently no approved or effective therapies for these disorders.

Obesity Caused by Downstream Genetic Deficiencies Affecting the MC4 Pathway

MC4 Heterozygous Deficiency Obesity

MC4 heterozygous deficiency is caused by the absence of one genetic copy of the gene for MC4R. Consistent with POMC heterozygous deficiency, MC4 heterozygous deficiency results in a strong predisposition to early onset and severe obesity. MC4 heterozygous deficiency is the most common genetic cause of obesity. An epidemiological study performed in Europe in 2006 reported a prevalence of 2.6% of genetic defects in the MC4 gene in the obese population with a BMI of greater than 30 kg/m^2 , and studies performed in both Europe and the United States in 2000 and 2003, respectively, reported a prevalence of up to 4% of these genetic defects in more severely obese populations with a BMI of greater than 35 kg/m^2 . These prevalence rates suggest that there are approximately one million people in the United States with obesity caused by a mutation of the MC4R gene.

These patients have a higher risk than the general population for early onset obesity and complications such as diabetes. Furthermore, MC4 deficiency may offset the beneficial effects of diet and exercise for sustained weight loss, limiting treatment options for these individuals. There are currently no approved or effective therapies for MC4 heterozygous deficiency obesity.

We believe that MC4 heterozygous deficient patients can respond to setmelanotide therapy by increasing activity that results from the one normal copy of the MC4 gene. However, while setmelanotide appears to show strong efficacy in a Phase 1b trial for the treatment of MC4 heterozygous deficiency obesity patients, we are focusing instead on genetic defects that are upstream of the MC4 receptor. This is because we believe that many of these upstream genetic disorders cause even more severe, often life-threatening obesity, and because setmelanotide has the potential to restore lost function in these upstream disorders, delivering more compelling efficacy.

Expanding Attention to the Diagnosis of Genetic Obesity

The Endocrine Society issued new Pediatric Obesity Guidelines in January 2017 that, for the first time, recommend genotyping patients with severe pediatric obesity and hyperphagia. These guidelines estimate that up to 7% of patients with extreme pediatric obesity have a genetic mutation, including genetic MC4 pathway deficiencies, that drives their obesity. The guidelines also suggest that this percentage of severe pediatric obesity patients will increase, with newer methods and wider awareness of the need for genetic testing.

We are supporting several initiatives to expand the diagnosis of genetic obesity, including The Genetic Obesity Project. The Genetic Obesity Project has initiated a genotyping study, or GO-ID genotyping study,

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and a patient registry, or GO-ID registry, both focusing initially on identifying people with POMC deficiency obesity and LepR deficiency obesity and which we intend to expand to include other MC4 pathway deficiencies. Our preliminary results in 560 genotyped patients suggest we can successfully identify these patients. We have also conducted a genetic obesity epidemiology analysis of MC4 pathway genetic defects in a large representative sample of the U.S. population. Based on preliminary findings from this analysis, we believe the prevalence of these MC4 pathway deficiencies could be substantially larger than our current estimates. Our work in the epidemiology for these rare genetic disorders of obesity is continuing.

Limitations of Current Therapies

Although drugs approved for general obesity can potentially be used in obese patients with MC4 pathway deficiencies, all have limited efficacy and aim to treat symptoms rather than addressing the underlying biology. There are currently no treatments approved specifically for obesity and hyperphagia in POMC deficiency obesity, LepR deficiency obesity, Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, or POMC epigenetic disorders. Bariatric surgery is not an option in patients with upstream defects in the MC4 pathway who have severe obesity and hyperphagia.

Setmelanotide: A First-in-Class MC4R Agonist in Two Phase 3 Programs

Setmelanotide is a potent, first-in-class, MC4R agonist peptide administered by daily subcutaneous, or SC, injection. Setmelanotide is in Phase 3 for the treatment of two rare genetic disorders of obesity caused by MC4 pathway deficiencies, and in Phase 2 for other MC4 pathway disorders. MC4R modulates a key pathway in humans that regulates energy homeostasis and food intake.

The critical role of the MC4 pathway in weight regulation was validated with the discovery that single genetic defects in this pathway result in severe, early onset obesity. The first generation MC4R agonists were small molecules that failed in clinical trials primarily due to safety issues, particularly increases in blood pressure, as well as limited efficacy. In contrast, setmelanotide is a peptide that retains the specificity and functionality of the naturally occurring hormone that activates MC4R. Approximately 275 obese subjects and patients have been treated with setmelanotide in previous and ongoing clinical trials in which setmelanotide demonstrated significant weight loss with good tolerability.

Clinical Development in Rare Genetic Disorders of Obesity Caused by MC4 Pathway Deficiencies

Setmelanotide is currently in Phase 3 development for the treatment of two ultra-rare monogenic disorders of obesity, POMC deficiency obesity and LepR deficiency obesity, each of which has had one pivotal trial. We are currently enrolling patients in our POMC deficiency obesity Phase 3 clinical trial, and expect to complete enrollment by the end of 2017 and to report Phase 3 data in the first half of 2019. We expect to enroll the first patient in our LepR deficiency obesity Phase 3 clinical trial in the second half of 2017, and to complete enrollment in 2018. In addition, setmelanotide is in Phase 2 development for the treatment of other rare monogenic disorders of obesity, including Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders. We hypothesize that all of these disorders are genetically defined deficiencies upstream in the MC4 pathway. We have initiated two very similar Phase 2 protocols, each of which is designed to capture a broad range of indications under one investigational protocol. We recently demonstrated preliminary proof of concept in Bardet-Biedl syndrome, indicating that this is also a setmelanotide-responsive, upstream MC4 pathway disorder. We are continuing to enroll patients in this trial and expect to report preliminary Phase 2 results in the fourth quarter of 2017. We expect to initiate a Phase 3 clinical trial in Bardet-Biedl syndrome in 2018. We expect to enroll patients with Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders in the second half of 2017 and to report preliminary results from these trials in the first half of 2018. We have also completed a Phase 2 trial in Prader-Willi syndrome, or PWS. Based on FDA consultations to date, and the FDA awarding breakthrough therapy designation, we believe we can seek indications for obesity caused by upstream defects in the MC4 pathway with faster paths to approval, as

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compared to typical obesity drug candidates, because of the high unmet need and rare prevalence of these disorders. We expect to use the results of our Phase 3 clinical trials of setmelanotide in POMC deficiency obesity and LepR deficiency obesity as the foundation for proceeding directly to approval for those indications.

We believe our data in POMC deficiency obesity, LepR deficiency obesity, and Bardet-Biedl syndrome provide strong proof of concept that setmelanotide, when targeted for deficiencies affecting the upstream portion of the MC4 pathway, can provide compelling efficacy for weight loss and decrease in hunger. Proof of concept for substantial weight loss in patients with downstream, heterozygous mutations of the MC4R gene itself has also been achieved in a small, four week, Phase 1b clinical trial. While these downstream defects are not our current area of focus, we believe they provide evidence for substantial, though lesser, weight loss efficacy in a setting of a partially defective, downstream defect in the MC4 pathway, which impacts a significantly larger population.

Initial setmelanotide clinical trials were in patients with general obesity, which provided preliminary evidence of the safety and efficacy of the drug, and were the foundation for the Phase 2 trials in rare genetic disorders of obesity. In these trials, setmelanotide has generally achieved weight loss without adversely increasing blood pressure. These trials in the general obese population are described separately below.

The following table outlines our ongoing and planned setmelanotide trials in rare monogenic disorders of obesity.

Setmelanotide: Key Clinical Programs in Monogenic MC4 Pathway Disorders of Defined Obesity

	POMC Deficiency Pivotal	LepR Deficiency Pivotal	POMC/LepR Deficiency Proof of Concept	Other Populations Proof of Concept Basket Protocols ⁽⁶⁾
Clinical trial phase	Phase 3	Phase 3	Phase 2	Phase 2
Status	Initiated 1Q2017	Initiated 2Q2017 ⁽⁵⁾	Initiated 2014, Completed 4Q 2016 for these indications	Initiated 2016 ⁽⁷⁾⁽⁸⁾
Treatment groups ⁽¹⁾	Setmelanotide ⁽²⁾	Setmelanotide ⁽²⁾	Setmelanotide	Setmelanotide
Number of patients	10 ⁽³⁾	10 ⁽³⁾	2 POMC, 3 LepR	20 ⁽⁹⁾
Patient demographics	Adult/pediatric POMC deficient ⁽⁴⁾	Adult/pediatric LepR deficient ⁽⁴⁾	Adults/Adolescents	Adult/pediatric ⁽⁴⁾ Multiple indications: Bardet-Biedl syndrome; Alström syndrome; POMC heterozygous deficiency obesity; POMC epigenetic disorders
Duration of treatment	52 weeks + Extensions	52 weeks + Extensions	12 weeks + Extensions	12 weeks + Extensions
Location	United States, Germany, United Kingdom, France	United States, Germany, United Kingdom, France ⁽¹⁰⁾	Germany	United States, Germany, United Kingdom, France

(1) Setmelanotide, administered as once daily SC injection.

(2) These trials include a placebo controlled, double-blind withdrawal period.

(3) Approximately 10 POMC deficiency obesity and 10 LepR deficiency obesity patients are anticipated in each pivotal trial.

(4) POMC deficiency includes homozygous deficiency in either the POMC or PCSK genes; pediatric patients ³ 12 years are currently being studied, and lower age pediatric patients will also be studied when applicable.

(5) Trial site activation activities ongoing and first enrolled patient anticipated by the second half of 2017.

(6) Basket protocols study a variety of different indications or patient populations administratively in one protocol, though each population is enrolled and analyzed separately.

(7) One of our proof of concept basket protocols was originally the Phase 2 trial for POMC deficiency obesity and LepR deficiency obesity initiated in Germany in 2016 and provided proof of concept in these indications. This trial was later amended in 2016 to

include other MC4 pathway disorders. Our second basket protocol is open, or is being opened in other geographical locations (United States 2016; United Kingdom, France in 2017).

- (8) We have enrolled Bardet-Biedl syndrome patients, and we anticipate enrolling patients in the other indications, Alström syndrome, POMC heterozygous deficiency obesity and POMC epigenetic disorders, by the fourth quarter of 2017.
- (9) Approximately five patients are planned for each of the four MC4 pathway indications.
- (10) We have ongoing trials in the United States and trial approvals are in process in Germany, United Kingdom, and France.

Setmelanotide: Clinical Development Program in Genetically Defined Obesity

Phase 2 Clinical Development in POMC Deficiency Obesity

We have completed a Phase 2 proof of concept, open label clinical trial, Study RM-493-011, in patients with POMC deficiency obesity. With the two patients in this trial, we have provided proof of concept for the compelling effect of setmelanotide in this disorder and after discussions with the FDA, have initiated a Phase 3 trial for this indication. To validate the scientific and clinical importance of our Phase 2 findings, the results of this trial were published on July 21, 2016 in the New England Journal of Medicine, and the accompanying editorial described the trial as demonstrating impressive hunger reduction and weight loss as well as improved insulin sensitivity.

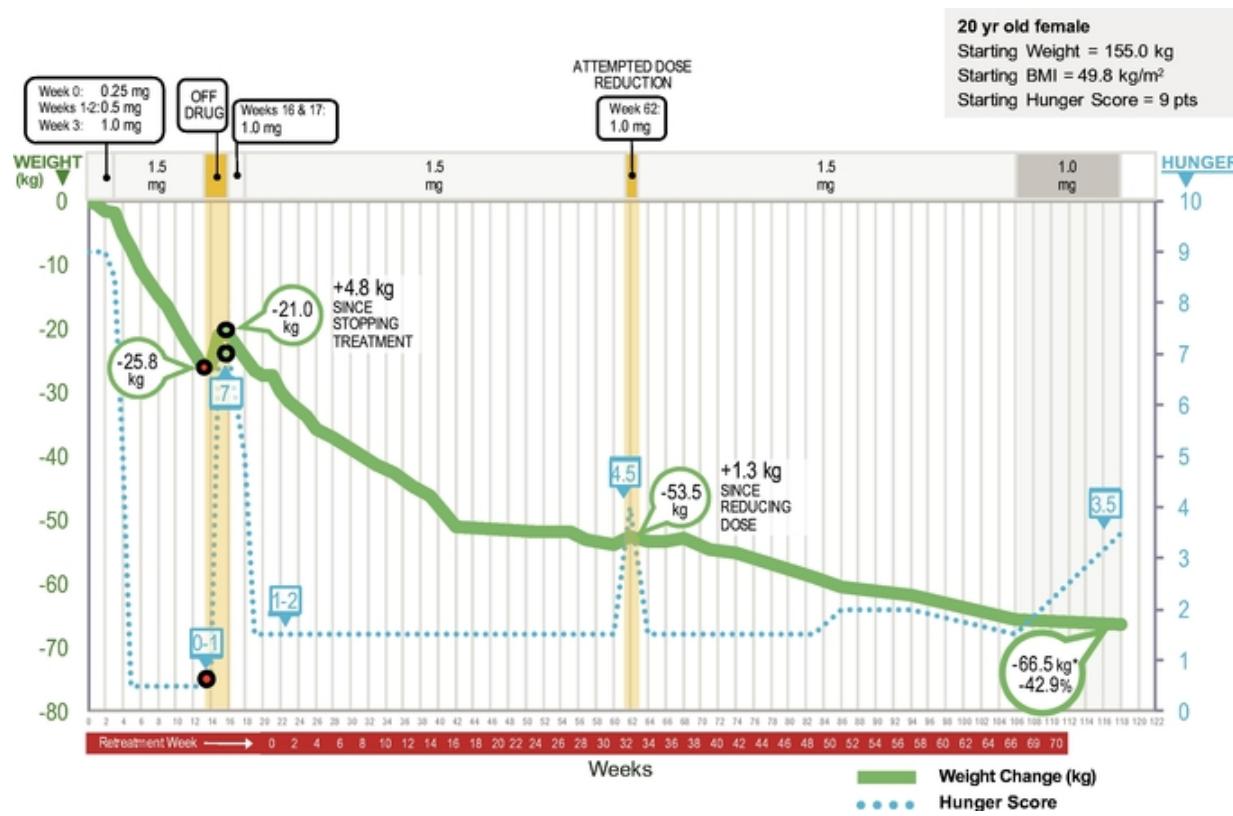
The first setmelanotide-treated patient was a 20-year old woman, who at three months of age experienced the onset of obesity and hyperphagia. In spite of enormous efforts, the patient was never able to stabilize her body weight, except for brief periods, and she has remained hyperphagic. Ahead of our trial, the patient's self-reported trial hunger score was eight to nine out of 10 points, representing extreme hunger. She was entered into the trial at adulthood because of her severe obesity, with a baseline weight of 155 kg, or 341.7 lbs., and a BMI of 49.8 kg/m², and significant risk of comorbidities and a reduced life expectancy.

The trial, initially a 13-week, open label, ascending dose Phase 2 trial, was approved by the German Federal Institute for Drugs and Medical Devices, with open-label one year extensions, and was planned to include approximately four to six patients with genetically confirmed POMC deficiency obesity. After efficacy-gated dose escalation, aiming for weekly weight loss of approximately two kg, or 4.4 lbs., the primary endpoint was weight loss, with other key endpoints including hunger score, body composition, insulin and glucose parameters, metabolic and cardiovascular risk factors, energy expenditure and general safety and tolerability.

After 13 weeks of therapy, with approximately the first four weeks at sub-therapeutic doses, our initial patient demonstrated weight loss of 25.8 kg, or 56.9 lbs., representing 16.7% of her initial body weight, with approximately two to three kilograms per week of weight loss demonstrated at the highest 1.5 mg/day dose. Hunger scores, measured using a Likert score of zero to 10, where zero represents no hunger and 10 represents extreme hunger, mirrored the rate of weight loss, moving from scores of eight to nine prior to our trial to zero to one, as the patient was treated with increasing doses of setmelanotide. After termination of the 13-week main trial, the patient underwent a three-week withdrawal period off drug and regained 4.8 kg, or 10.6 lbs., with a return to moderate to severe hunger. Following approval to restart setmelanotide treatment, there was an immediate reduction of hunger and subsequently a continuation of body weight loss. This patient was on continuous treatment for 106 weeks, with a total weight loss of 65.6 kg, or 144.6 lbs., representing 42.3% of her initial body weight. There was no apparent difference in the rate of weight loss during the initial extension phase versus the main trial, however over time, the rate of weight loss has slowed, though this patient has continued to lose weight. The patient's need for continued therapy was supported by a short period of withdrawal after the patient had been treated for over one year. Reducing her daily dose from 1.5 mg/day to 1.0 mg/day resulted in an increase in her hunger scores from one to two points to four to five points, resulting in the patient requesting to be returned to her 1.5 mg/day dose, after which her hunger scores returned to one to two points. This data supports the physiological prediction that pharmacological treatment for this condition to suppress hunger will be required chronically. After approximately 106 weeks of treatment, her dose was reduced to 1 mg/day, and while her weight remained stable from week 106 to week 118, her hunger scores increased to three to four points on the lower dose.

The results for this patient are shown in the figure below.

Initial Patient in the Setmelanotide POMC Deficiency Obesity Phase 2 Trial⁽¹⁾



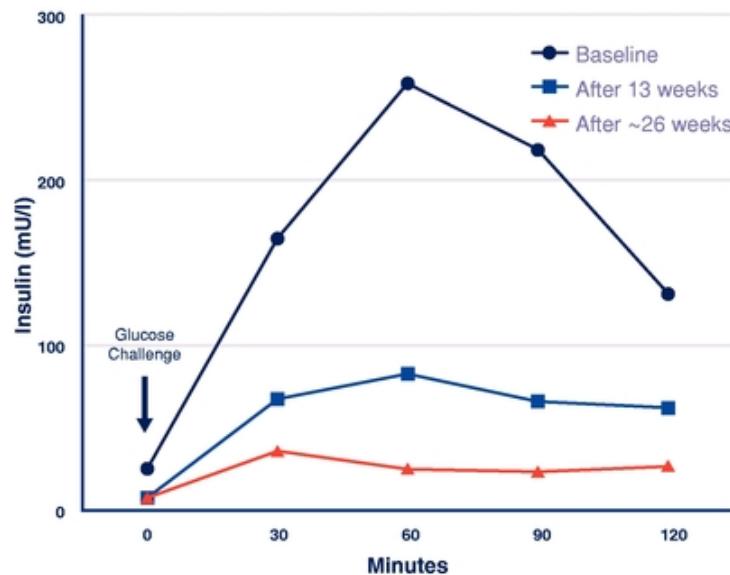
* Figures represent cumulative weight lost in kgs.

(1) Daily setmelanotide dose adjustments over time are indicated at the top of the panel.

In general, diet induced weight loss in patients with general obesity is accompanied by significant counter-regulatory effects, including reductions in energy expenditure and increases in hunger. These lead to weight regain in the majority of patients. In contrast, the initial patient in our trial did not manifest these counter-regulatory responses, even after six months of therapy and a tremendous reduction of body weight. This data supports an effect of setmelanotide on energy expenditure independent from the profound effects on hyperphagia, corroborating results from previous trials of setmelanotide in patients with general obesity. Also of note, the reduction in body weight was mainly due to a loss of body fat mass, and lean body mass was not greatly altered. In this initial patient, setmelanotide was also associated with excellent tolerability, additional favorable changes in cardiovascular risk parameters, or lipids, and improvements in blood pressure and heart rate.

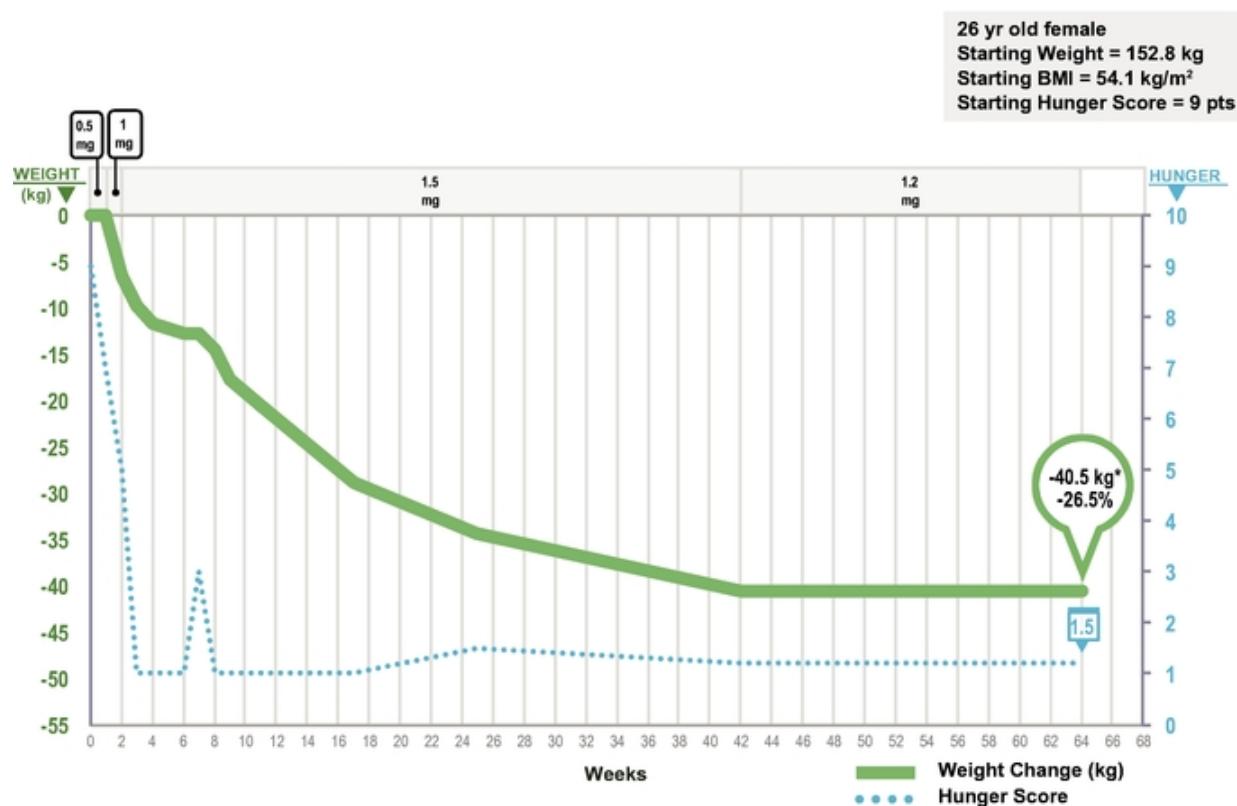
MC4R activation also causes improvements in glucose and insulin parameters in animal models, independent of weight loss. As shown in the figure below, for the initial patient in our POMC deficiency proof of concept trial, setmelanotide demonstrated a marked improvement in insulin resistance during treatment. While weight loss likely played an important role in this improvement, we believe the independent effect of MC4R agonism may also have contributed.

Setmelanotide Treatment Effects on Insulin Resistance (Insulin Response in Oral Glucose Tolerance Test) at Baseline, After 13 Weeks of Treatment (Phase 1), and at Approximately 26 Weeks During the Long-term Extension for our POMC Initial Patient



Results are also available for treatment with setmelanotide of a second patient with POMC deficiency obesity. The second patient is a 26-year old woman who also experienced early onset of obesity and hyperphagia. Like the first patient, in spite of significant efforts, she was never able to stabilize her body weight, and she has remained hyperphagic. Ahead of our trial, the patient's self-reported trial hunger score was nine out of 10 points, representing extreme hunger, and her weight and BMI at trial entry were 152.8 kg, or 336.9 lbs., and 54.1 kg/m^2 , respectively.

After 42 weeks of therapy at the 1.5 mg/day dose, our second patient demonstrated weight loss of 40.6 kg, or 89.5 lbs., representing 26.6% of her initial body weight, with approximately two to three kilograms per week of weight loss demonstrated initially. Hunger scores, measured using a Likert score of zero to 10, where zero represents no hunger and 10 represents extreme hunger, mirrored the rate of weight loss, with scores moving from nine prior to the trial to one on most weeks during the trial, as the patient was treated with increasing doses of setmelanotide. Similar to the initial patient, setmelanotide demonstrated an improvement in insulin resistance during treatment in our second POMC deficiency obesity patient. This patient continues on active treatment, with a total of 64 weeks on therapy, although this patient is now on a reduced 1.2 mg/day dose, and her weight has stabilized at a weight loss of 40.5 kg, or 89.3 lbs.

Our Second Patient in the Setmelanotide POMC Deficiency Obesity Phase 2 Trial⁽¹⁾

* Figures represent cumulative weight lost in kgs.

(1) Daily setmelanotide dose adjustments over time are indicated at the top of the panel.

Setmelanotide was generally well tolerated in the POMC deficiency obesity Phase 2 trial, with few adverse events, all mild and infrequent, and all previously reported in other clinical trials. These included reduced appetite and tanning of skin and nevi, or moles, intermittent and mild injection site reactions, and in rare instances tiredness, dry mouth, and gastrointestinal symptoms. The single serious adverse event was an influenza immunization reaction, which resulted in an overnight hospitalization and was considered unrelated to trial drug. A similar immunization reaction had occurred in this patient in a previous influenza immunization prior to treatment, and the patient has continued on setmelanotide since that event.

The results from the initial patients in our POMC deficiency obesity proof of concept trial are compelling, but these data have limitations due to open label treatment. However the strong treatment effect is supported by these patients' long histories of weight gain and hyperphagia prior to treatment, and a strong dose response in the dose escalation phase. More importantly, the biology of this disorder has been well studied, and the clinical responses in these patients were strongly predicted by the deep understanding of the role of the MC4 pathway in appetite and weight regulation. The interruption of treatment effectively allowed the first patient to serve as her own control, demonstrating an immediate and rapid increase in hunger and weight after a short-term treatment withdrawal, and a rapid response to re-treatment, thereby further demonstrating the strong effect of setmelanotide. The greater than two years of treatment of our first patient, and the greater than one year of treatment for our second patient also support the ability of setmelanotide to be effective for longer treatment periods. Finally, our data supports that this indication will require chronic treatment.

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Most importantly, this initial proof of concept data provides support for the belief that setmelanotide will restore activity in patients with upstream defects in the MC4 pathway, by helping patients lose weight and reduce hyperphagia. This was confirmed in our second MC4 pathway rare genetic obesity, LepR deficiency obesity. Similarly, we would expect efficacy in other upstream MC4 pathway genetic disorders, many of which are under study in Phase 2 proof of concept trials.

Phase 3 Clinical Development in POMC Deficiency Obesity

After discussions with the FDA as part of our breakthrough therapy designation, we initiated our Phase 3 trial in POMC deficiency obesity in January 2017, Study RM-493-012. This is an open label, one-year trial, including a double-blind placebo-controlled withdrawal period, of setmelanotide in POMC deficiency obesity. This pivotal trial will assess long-term efficacy of setmelanotide given once daily by SC injection. The trial will begin with an initial period of dose titration lasting between two and 12 weeks where the individual patient's therapeutic dose will be established by upwards dose titration in two week intervals. Thereafter, patients will continue on active treatment at their individually titrated optimal therapeutic dose for an additional 10 weeks, for a total combined dosing duration of 12 weeks at the individual patient's therapeutic dose. Patients who demonstrate at least five kilograms weight loss at the end of the open label treatment period will continue onto the double-blind, variably-timed, placebo-controlled, withdrawal period lasting eight weeks inclusive of a four-week period of placebo treatment. Following the withdrawal period, all patients will complete an additional period of setmelanotide treatment to bring the total therapeutic dosing period to one year.

We plan to treat approximately 10 patients in this trial. We will initially enroll patients aged 12 years and older, but, subject to FDA approval, intend to amend the protocol to include patients aged six years and older before completion of the trial. The primary endpoint of the trial will be percent change in body weight over one year, with key secondary endpoints of safety and tolerability, hunger, change in body fat mass and glucose parameters, and the effect of withdrawal of setmelanotide in the double-blind, placebo controlled period. We have also obtained Scientific Advice for this protocol from the European Medicines Agency, or EMA, and the trial is currently enrolling in the United States, United Kingdom, and Germany, and has been approved in France.

We expect to complete enrollment by the end of 2017, and to report Phase 3 data in the first half of 2019.

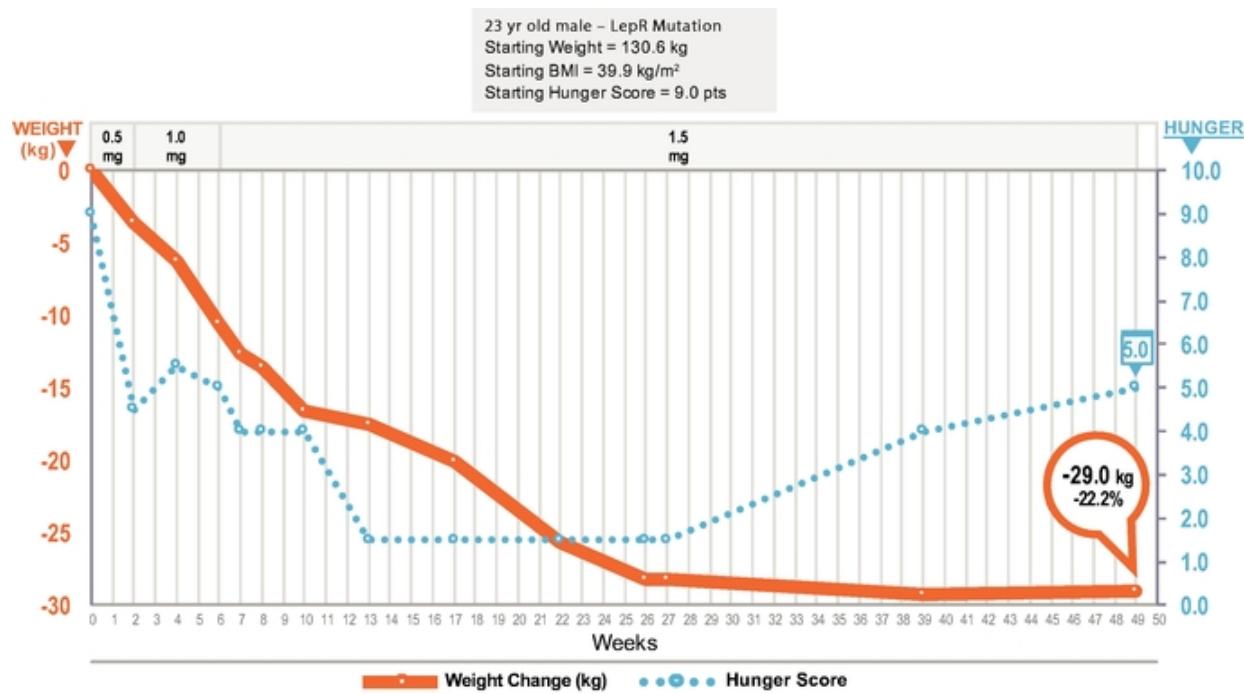
Phase 2 Clinical Development in LepR Deficiency Obesity

Leptin's role in obesity has been elucidated by characterization of severely obese people with homozygous mutations that impair the activity of leptin, including disruption of signaling at the LepR, known as LepR deficiency obesity. To study setmelanotide in this indication we initially amended our Phase 2 clinical trial in POMC deficiency obesity, Study RM-493-011, to also include this new and related genetically defined population of severely obese patients. We then completed this part of the Phase 2 proof of concept, open label clinical trial in patients with LepR deficiency obesity by treating three patients in this trial, who demonstrated weight loss and hunger reduction as outlined below.

Results from treatment with setmelanotide in these three LepR deficiency obesity patients are available. The first LepR deficiency obesity patient was a 23-year old male, who experienced early onset of obesity and hyperphagia. After little success in controlling his weight, he underwent, and failed, a gastric banding procedure, and had regained over 20 kg in the last year since his procedure. Ahead of our trial, the patient's self-reported trial hunger score was nine out of 10 points, representing extreme hunger, and his weight and BMI at trial entry were 130.6 kg, or 287.9 lbs., and 39.9 kg/m², respectively. After initiation and upwards dose titration over 13 weeks of setmelanotide treatment, the patient demonstrated prompt and striking reductions in appetite and body weight with a total loss of 17.5 kg body weight, representing 13.4% of his initial body weight. Hunger scores decreased from nine points at baseline to one to two points

at 13 weeks. With continued treatment for 27 weeks, the patient lost 28.2 kg, or 62.2 lbs, representing 21.6% of his initial body weight, and during that interval, he had a hunger score of one to two. Subsequently, on this dose, his weight has been generally stable through 49 weeks of treatment. The weight loss was predominantly caused by a reduction in body fat and resting energy expenditure stayed stable during this period. This patient also had pre-trial insulin levels that were elevated as examined by an oral glucose tolerance test, as were glucose values, demonstrating insulin resistance. These values improved with setmelanotide treatment. Notably, there was also an improvement in the patient's lipid profile over 13 weeks of setmelanotide treatment. Setmelanotide was generally well tolerated in this LepR deficiency obesity trial.

Initial Patient in the Setmelanotide LepR Deficiency Obesity Phase 2 Trial⁽¹⁾



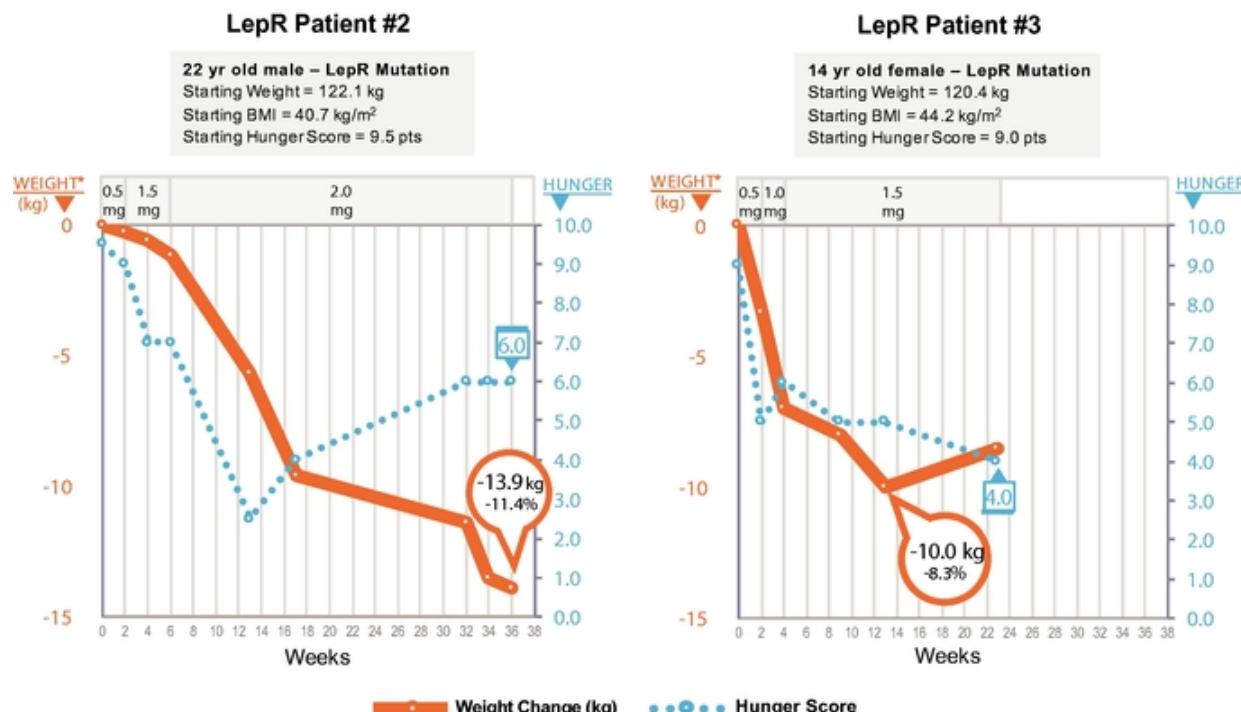
* Figures represent cumulative weight loss in kgs.

(1) Daily setmelanotide dose adjustments over time are indicated at the top of the panel.

The second LepR deficiency obesity patient is a 22-year old male who also experienced early onset of obesity and hyperphagia. His growth curve since infancy demonstrated early onset, severe obesity that had continued through his whole life, with little ability to control his weight gain. Ahead of our trial, the patient's self-reported trial hunger score was nine to 10 out of 10 points, and his weight and BMI at trial entry were 122.1 kg, or 269.2 lbs., and 40.7 kg/m², respectively. He was treated with setmelanotide and his dose was escalated up to 1.5 mg once daily with only modest effects on weight and hunger scores. However, when he was advanced to 2 mg once daily, he demonstrated prompt and striking reductions in appetite and body weight. After 17 weeks, including 11 weeks on his therapeutic dose of 2 mg/day, he had lost 9.6 kg, or 21.2 lbs, representing 7.9% of his body weight, and his hunger score dropped to two to three points. By 36 weeks of total treatment, he had lost 13.9 kg, or 30.6 lbs, representing 11.4% of his body weight. Despite good tolerance of treatment and this marked weight loss, the patient self-discontinued the drug starting at week 36 for approximately two weeks. During this time he regained 5.2 kg or 11.5 lbs, and his hunger score increased to nine out of 10 points, or severe hunger. The patient reported that he felt hungry every hour, and was struggling not to eat. As a result, treatment was re-initiated at the 2 mg dose, and was then

increased to 2.5 mg per day with the goal of accelerating his weight loss. Following the increase, he demonstrated a significant reduction in hunger, with his hunger scores decreasing from nine to two out of 10 points, and a reduction in body weight. The patient remains on treatment with good tolerability. This patient had few metabolic abnormalities at baseline, but he was hyperinsulinemic as examined by an oral glucose tolerance test. After 13 weeks of treatment, the hyperinsulinemia started to improve and the blood glucose levels during the oral glucose tolerance test normalized.

Our Second and Third Patients in the Setmelanotide LepR Deficiency Obesity Phase 2 Trial⁽¹⁾



* Figures represent cumulative weight loss in kgs

* Figures show patient data only during weeks in which patients were in compliance with the trial protocol.

(1) Daily setmelanotide dose adjustments over time are indicated at the top of the panel.

The third LepR deficiency obesity patient is a 14-year old female adolescent, and the first adolescent patient treated with setmelanotide. Her growth curve since infancy demonstrated early onset, severe obesity her whole life, with little ability to control her weight gain. Ahead of our trial, the patient's self-reported trial hunger score was nine out of 10 points, and her weight and BMI at trial entry were 120.4 kg, or 265.4 lbs., and 44.2 kg/m², respectively. The patient lost 10 kg, or 22 lbs, representing 8.3% of her body weight, and her hunger score reduced to five out of 10 points in the first 13 weeks on a dose of 1.5 mg per day. Before and during treatment, the patient showed adolescent behavior that compromised compliance with the treatment regimen. This behavior led to a misunderstanding that, by week 23 of the treatment, resulted in the patient incorrectly performing the injections late in the afternoon and at an incorrect, lower dosage of 1.0 mg. The combination of the minimum dose threshold for therapeutic effects and the half-life of setmelanotide being 10 to 12 hours meant that the combination of lower dose and the maximum drug concentration being reached during the night resulted in an interval of less-optimal outcomes and weight regain. The patient reported that her hunger was less intensive during the night but increased during the day. Eventually, these errors were reported and corrected. Following such correction,

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careful monitoring was instituted to ensure that the patient performed the injections in the morning as instructed and the dosage was increased to 2.0 mg per day.

This trial provides the second proof of concept for the effectiveness of setmelanotide in patients with upstream defects in the MC4 pathway, showing marked weight reduction and decreases in hunger in patients with LepR deficiency obesity. In addition, the efficacy of the drug correlates well with periods of setmelanotide treatment and withdrawal, as in POMC deficiency obesity. Based on this proof of concept for the compelling efficacy of setmelanotide in this disorder, we have transitioned the LepR development program to Phase 3.

Phase 3 Clinical Development in LepR Deficiency Obesity

Our LepR deficiency obesity development program is now in Phase 3. We expect to enroll our first patient in our LepR deficiency obesity Phase 3 clinical trial in the second half of 2017, and to complete enrollment in 2018. This is an open label, one-year trial, including a double-blind placebo-controlled withdrawal period, of setmelanotide in LepR deficiency obesity. This pivotal trial will assess long-term efficacy of setmelanotide given once daily by SC injection in LepR deficiency obesity, and is planned to be very similar to the Phase 3 ongoing trial in POMC deficiency obesity. The trial will begin with an initial period of dose titration lasting between two and 12 weeks where the individual patient's therapeutic dose will be established by upwards dose titration in two week intervals. Thereafter, patients will continue on active treatment at their individually titrated optimal therapeutic dose for an additional 10 weeks, for a total combined dosing duration of 12 weeks at the individual patient's therapeutic dose. Patients who demonstrate at least five kilograms weight loss at the end of the open label treatment period will continue onto the double-blind, variably-timed, placebo-controlled, withdrawal period. Following the withdrawal period, all patients will complete an additional period of setmelanotide treatment to bring the total therapeutic dosing period to one year.

We plan to treat approximately 10 patients in this trial, aged 12 years and older, and subject to FDA approval, we intend to amend the protocol to include patients aged six years and older before completion of the trial. The primary endpoint of the trial will be percent change in body weight over one year, with key secondary endpoints of safety and tolerability, hunger, change in body fat mass and glucose parameters, and the effect of withdrawal of setmelanotide in the double-blind, placebo controlled period. We have submitted this trial to the FDA, and will also conduct the trial in the United Kingdom, France and Germany.

Based on the FDA awarding breakthrough therapy designation for the treatment of obesity associated with genetic defects upstream of the MC4 receptor in the leptin-melanocortin pathway, which includes the LepR deficiency obesity indication, we believe we can seek indications for this type of obesity with a faster path to approval, as compared to typical obesity drug candidates, because of the high unmet need and rare prevalence of this disorder.

Phase 2 Clinical Development in Bardet-Biedl Syndrome

Bardet-Biedl syndrome is a life-threatening, orphan disease with prevalence of approximately one in 100,000 in North America. We estimate that the addressable patient population for Bardet-Biedl syndrome is approximately 1,500 to 2,500 patients in the United States. It is a rare monogenic disorder that causes severe obesity and hyperphagia as well as vision loss, polydactyly, kidney abnormalities, and other signs and symptoms. Bardet-Biedl syndrome is part of a class of disorders called ciliopathies, or disorders associated with the impairment of cilia function in cells. Cilia are hair-like cellular projections that play a fundamental role in the regulation of several biological processes, including satiety signaling. Cilia dysfunction is thought to contribute to hyperphagia and obesity in Bardet-Biedl syndrome. Bardet-Biedl syndrome is a genetically heterogeneous disease that is caused by as many as 21 separate Bardet-Biedl loci defects resulting in a similar syndrome, though each Bardet-Biedl syndrome patient only has one of these defects.

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The role of abnormal cilia development and function in obesity has been elucidated in animal models, most strongly for Bardet-Biedl. Studies in mouse models of Bardet-Biedl syndrome show that deficiencies in the MC4 pathway contribute to the obesity and hyperphagia in Bardet-Biedl syndrome, with animals developing hyperphagic tendencies early in life. Notably, these mice have decreased leptin receptor signaling, with the essential hallmarks of failure to activate POMC neurons. This is supported in Bardet-Biedl syndrome rodent models, where the mice respond to an MC4 agonist resulting in reduced food intake and body weight. The relation of Bardet-Biedl syndrome gene mutations to the MC4 pathway is supported by clinical data. Patients with Bardet-Biedl syndrome have higher leptin than expected for their degree of adiposity, or leptin resistance, which is consistent with the notion that ciliopathy-induced leptin signaling dysfunction is associated with leptin resistance.

Overall, these data support that the phenotypes of these ciliopathies, while complex with additional clinically important features along with obesity and hyperphagia, may be responsive to setmelanotide treatment, and will be investigated in our proof of concept Phase 2 trial.

We are studying Bardet-Biedl syndrome patients who are severely obese, or whose BMI is equal to or greater than 40kg/m², to provide proof of concept that Bardet-Biedl syndrome patients will also demonstrate decreased hunger and significant weight loss, similar to that seen in patients with POMC deficiency obesity, or LepR deficiency obesity. We have enrolled the first five patients in this trial, and plan to enroll additional patients for this indication in the second half of 2017 at sites in the United States and possibly Europe. We anticipate reporting preliminary results for Bardet-Biedl syndrome in the fourth quarter of 2017, and to initiate Phase 3 clinical trials in 2018.

For this trial, additional assessments of hunger using daily hunger scores and questionnaires were also obtained. We plan to use these new assessments in our ongoing Phase 2 and Phase 3 trials and for future trials. These new assessments are as follows:

- Daily Hunger Scores. In addition to our morning assessment of hunger, as performed in the Phase 2 trials in POMC deficiency obesity and LepR deficiency obesity, we are also obtaining a daily hunger score rating in response to the question: "In the last 24 hours, how hungry did you feel when you were the *most* hungry?" Patients are asked to give a response that is measured on a scale of 0-10, whereby 0 points signifies "not hungry at all" and 10 points indicates the patient feels his or her "hungriest possible."
- Questionnaires. For patients 16 years of age and younger, we are using two observer related questionnaires as exploratory endpoints. These questionnaires are completed by the patient's parent or other caregiver.
 - The Food Problem Diary, or FPD, is based on food-related behaviors. This questionnaire was adapted from a similar questionnaire that was used with patients with Prader-Willi syndrome. The questionnaire is rated on a 30-point scale where 30 points is strong evidence of hyperphagia and 0 points is evidence of no hyperphagia. The best possible response therefore is 0 points.
 - The Significant Event Questionnaire, or SEQ, counts events not typically seen in this population, such as a patient leaving food on his or her plate at a meal. This questionnaire consists of eight "yes" or "no" questions. The best possible response is 8 points, since this questionnaire tracks events and behavior not typically seen in patients with MC4 pathway disorders. In contrast with other score scales, a higher score in this hunger assessment category represents improvement, and thus, the results are plotted in reverse scale and downward trends indicate improvement.

We believe that proof of concept in Bardet-Biedl syndrome has been demonstrated by improvements in hunger and weight reduction, supporting that this is a setmelanotide-responsive, MC4 pathway disorder. Four different Bardet-Biedl genotypes were studied in this trial. The age of

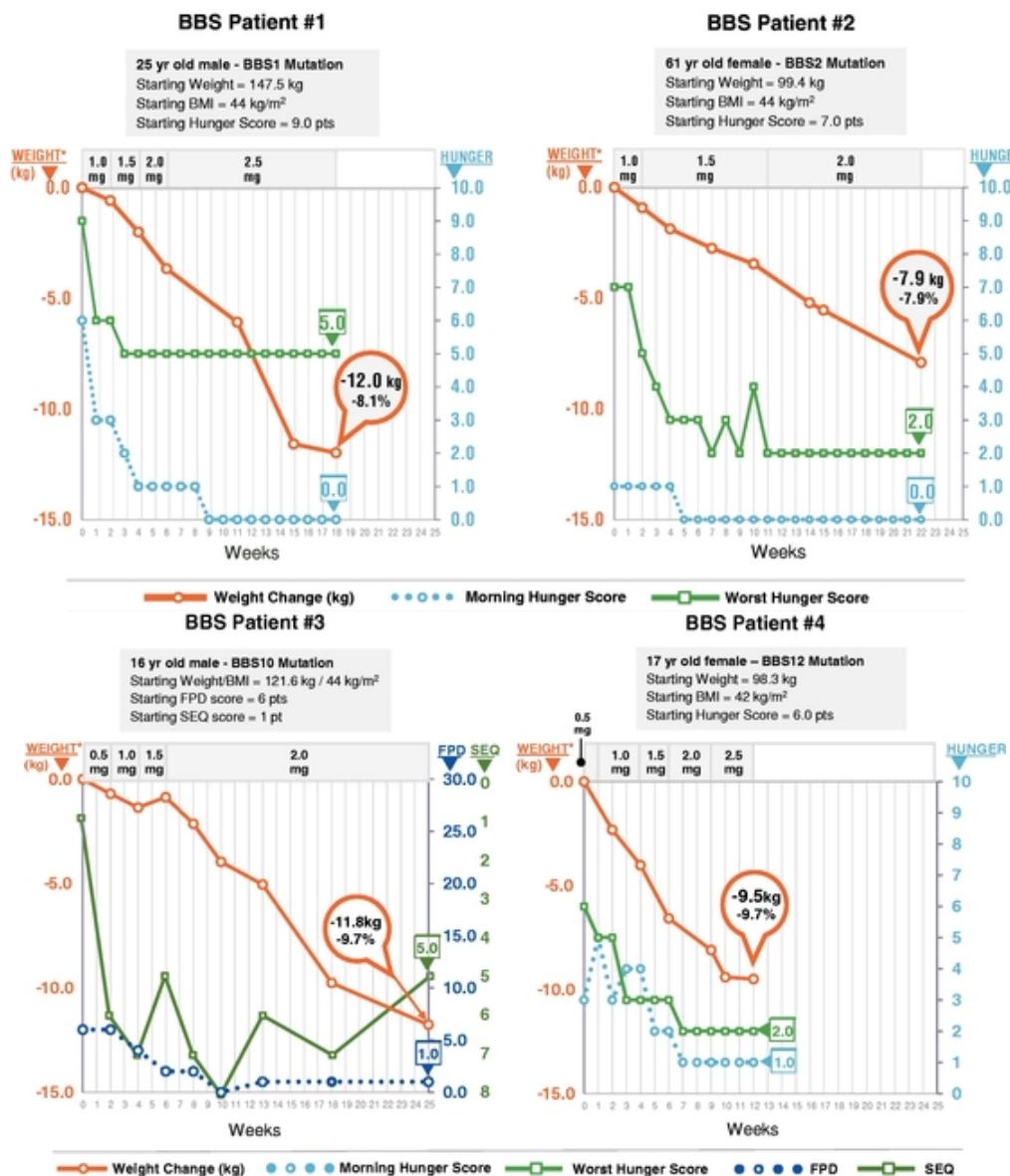
the patients ranged from 12 to 61 years of age. The starting weights of the patients ranged from 98.3 to 147.5 kg and BMI ranged from 42 to 49. The starting hunger scores for the adult patients ranged from 6 to 9 points on the 10-point scale, with higher scores indicating more hunger and the SEQ scores for the two adolescent patients were both 1.

Description of the Five Bardet-Biedl patients in the Phase 2 Proof of Concept study

Patient Number	Age (yrs)	Bardet-Biedl Type	Starting Weight (kg)	Starting BMI	Starting Hunger Score
1	25	1	147.5	44	Most hungry score = 9
2	61	2	99.4	44	Most hungry score = 7
3	16	10	121.6	44	FPD = 6/ SEQ = 1
4	17	12	98.3	42	Most hungry score = 6
5	12	1	119.3	49	FPD = 15/SEQ = 1

The Bardet-Biedl syndrome patients were treated with setmelanotide for a range of 12 to 25 weeks. Within that period, five to 14 weeks represented time spent in the dose titration period designed to define an individualized therapeutic dose. Two of the five patients remain in the titration phase. Four of the five patients showed early, but significant weight loss of 12.0, 7.9, 11.8 and 9.5 kg lost or 26.5, 17.4, 26.0, and 21.0 lbs. All five patients showed clear improvements in every hunger assessment. The outlier patient, patient #5 had marked improvements in hunger assessments. This patient's FPD improved from a baseline of 15 points to 7 points, and her SEQ improved from a baseline of 1 point to the maximum value of 8 points. The fifth patient did not show any reduction in weight, but rather presented a gain of 2.2 kg, or 4.9 lbs. over 18 weeks. This patient was a 12-year old with Type 1 diabetes who entered the trial with extremely poor glucose control (HbA1c, or an average blood sugar level, of = 10.1%). We are investigating the reason for the disconnect between her improvement in hunger and lack of weight loss, but it was noteworthy that during treatment her diabetes was better controlled, and her HbA1c showed a large improvement to 7.6%. Setmelanotide was generally well tolerated in the Bardet-Biedl syndrome Phase 2 proof of concept study.

Our Four Patients in the Setmelanotide Bardet-Biedl Syndrome Phase 2 Trial who showed improvements in both weight and hunger⁽¹⁾⁽²⁾



* Figures represent cumulative weight lost in kgs

FPD: Food Problem Diary; Score Range 0 to 30, higher score means worse result

SEQ: Significant Event Questionnaire, which counts significant food behaviour events rarely seen in this population (Y/N for 8 behaviours), so maximum score of 8 points means greatest improvement. Shown in reverse scale so downward movement equals improvement for clarity.

- (1) Daily setmelanotide dose adjustments over time are indicated at the top of the panel.
- (2) In some cases, dates for entry of weight and hunger assessment data may differ within a single patient.

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Phase 2 Proof of Concept Studies Focused on Patients with Monogenic Disorders of the MC4 Pathway: Alström syndrome, Heterozygous Mutations in the MC4 Pathway, and Epigenetic Disorders of the MC4 Pathway

We are conducting Phase 2, proof of concept trials in a variety of monogenic, upstream disorders of the MC4 pathway, including Alström syndrome, POMC heterozygous mutations in the MC4 pathway, and epigenetic disorders of the MC4 pathway. These trials are Phase 2 open label, single arm, proof of concept trials assessing the effect of setmelanotide on the rare genetic disorders of obesity described below. We hypothesize that all of these disorders may be genetically-defined deficiencies upstream in the MC4 pathway. Each trial includes a three month proof of concept phase at which weight loss, hunger and other metabolic parameters will be evaluated. If patients demonstrate significant weight loss and acceptable safety and tolerability, they will continue in one-year extensions for evaluation of setmelanotide's effects at one year and onwards of total therapeutic dosing. Similar to our previous trials, this trial will begin with an initial period of dose titration where the individual patient's therapeutic dose will be established by upwards dose titration in two week intervals. We plan to enroll approximately five patients for each of these rare genetic populations. We will conduct these trials, as well as the ongoing Bardet-Biedl syndrome trial described above, under basket protocols, which are designed to capture a broad range of patient populations to be treated under one investigational protocol. We believe this approach is efficient for studying many potential indications, and we intend to add additional populations to these basket protocols over the next one to two years.

The genetic disorders we are studying in our additional Phase 2 proof of concept trials are outlined below.

a. Clinical Development in Alström Syndrome Obesity

Alström syndrome is a life-threatening, ultra-rare orphan disease with a prevalence of approximately one in 1,000,000 in North America and we estimate that the addressable patient population for Alström syndrome obesity is approximately 500 to 1,000 patients worldwide. Alström syndrome shares many clinical features with Bardet-Biedl syndrome, including obesity and hyperphagia, and is also characterized by progressive vision loss, deafness, congestive heart failure, hyperinsulinemia and type 2 diabetes mellitus. Similarly, Alström syndrome is a ciliopathy caused by mutations in the ALMS1 gene, which has also been shown to be important for cilia function. Like Bardet-Biedl syndrome, recent scientific studies identify genetic deficiencies affecting the MC4 signaling pathway as a potential cause of the obesity and hyperphagia associated with Alström syndrome. Studies in a mouse model of Alström syndrome show a reduction in the number of cilia in specific neurons in the hypothalamus that are critical for MC4 pathway signaling. While Alström syndrome is less well studied than Bardet-Biedl syndrome, the similar pathophysiology of ciliary dysfunction and clinical presentation support that deficiencies in the MC4 pathway are implicated in the obesity and hyperphagia observed in Alström syndrome. Therefore, we hypothesize that setmelanotide treatment can be applied to treat Alström syndrome.

We will enroll Alström syndrome patients who are severely obese, or whose BMI is equal to or greater than 40kg/m², to provide proof of concept that Alström syndrome patients will also demonstrate decreased hunger and significant weight loss, similar to that seen in patients with POMC deficiency obesity, or LepR deficiency obesity. We plan to enroll our first patients for this indication in the second half of 2017 at sites in the United States and Europe, and to complete enrollment in 2018. We expect to report preliminary results in the first half of 2018.

b. Clinical Development in MC4 Pathway Heterozygous Deficiency Obesity

MC4 pathway heterozygous deficiency obesity is caused by the loss of one of the two genetic copies of either the genes for POMC, PCSK, or LepR. Animal models support that such heterozygous

deficiency in the critical leptin-melanocortin pathway can result in a strong predisposition to severe obesity. The effect of genetic heterozygous deficiency obesity was first demonstrated for another gene in the MC4 pathway: MC4R heterozygous deficiency obesity. Later data also supported that POMC heterozygous deficiency obesity also results in a strong predisposition to obesity, though the epidemiology and clinical characterization of these patients is less well known. An estimated 2% of severe, early onset obesity patients have POMC heterozygous deficiency obesity, which is much more common than the ultra-rare POMC deficiency obesity in which both copies of either the POMC or PCSK genes are impaired. Our initial clinical focus will be on the most severely obese MC4 pathway heterozygous patients to test the hypothesis that severely obese heterozygous POMC patients might also respond substantially to setmelanotide treatment.

We will study patients who are severely obese, or whose BMI is equal to or greater than 40kg/m², and who are heterozygous deficient for POMC. These patients have a heterozygous genetic mutation of the POMC or PCSK gene resulting in full or partial loss of MC4 pathway signaling to the downstream MC4R. The purpose of studying these patients in this trial is to provide proof of concept that severely impaired MC4 pathway heterozygous deficiency obesity patients will also demonstrate significant weight loss, similar to though possibly of less magnitude, as that seen in patients with POMC deficiency obesity or LepR deficiency obesity. We plan to enroll our first patients for this indication in the second half of 2017 at sites in the United States and Europe, and to complete enrollment in 2018. We expect to report preliminary results in the first half of 2018.

Of particular interest to us are mutations to the section of the POMC gene that is translated into the protein, beta-melanocyte stimulating hormone (b-MSH). These mutations have been implicated in human and canine obesity. In 2002, researchers identified one specific heterozygote mutation of b-MSH, called the R236G mutation, in two children with extreme childhood obesity. This R236G mutation results in an abnormal b-MSH protein with a markedly reduced ability to activate the MC4R itself, and may also prevent other natural MC4R ligands from activating the MC4R. These combined effects may result in more significant obesity than other heterozygous mutations. The overall prevalence of this mutation is rare, 0.7% of the obese population is estimated to carry this mutation, but our genotyping study of 560 patients with early onset, childhood obesity has identified five heterozygote patients with the R236G mutation, all with severe obesity. Because, in both our genotyping study and in the scientific literature, this mutation is associated with severe obesity and has a relatively-high observed prevalence, this mutation will be a focus when enrolling our Phase 2 trial in POMC heterozygous obesity.

We also plan to study patients who are heterozygous deficient for LepR deficiency obesity in the near future, though we have not yet initiated study in this population. Less is known about the epidemiology and clinical impact of LepR heterozygous deficiency obesity. In addition, we have hypothesized that patients who are composite heterozygous, or who have heterozygosity in two of the genes of the MC4 pathway, both POMC and LepR, and who therefore might have some impairment at more than one location in the MC4 pathway, might also be responsive to setmelanotide. We plan to begin studying these composite heterozygous patients at a future date.

c. Clinical Development in Patients with Epigenetic Changes at the POMC receptor

In our proof of concept Phase 2 trials, we also plan to study patients suffering from obesity due to a partial lack of MSH due to an epigenetic POMC variant. Epigenetics changes are DNA modifications that can change gene expression without altering the DNA sequence itself. The most stable epigenetic modification is called DNA methylation. Recently, our academic collaborators in Berlin have described a POMC hypermethylation variant, which correlates with increased body weight in children and adults. Therefore, the presence of the POMC genetic/epigenetic variant leads to an increased risk for obesity based on reduced POMC gene activity. We expect that these patients under express the POMC gene product and as a result have a partial MSH deficiency.

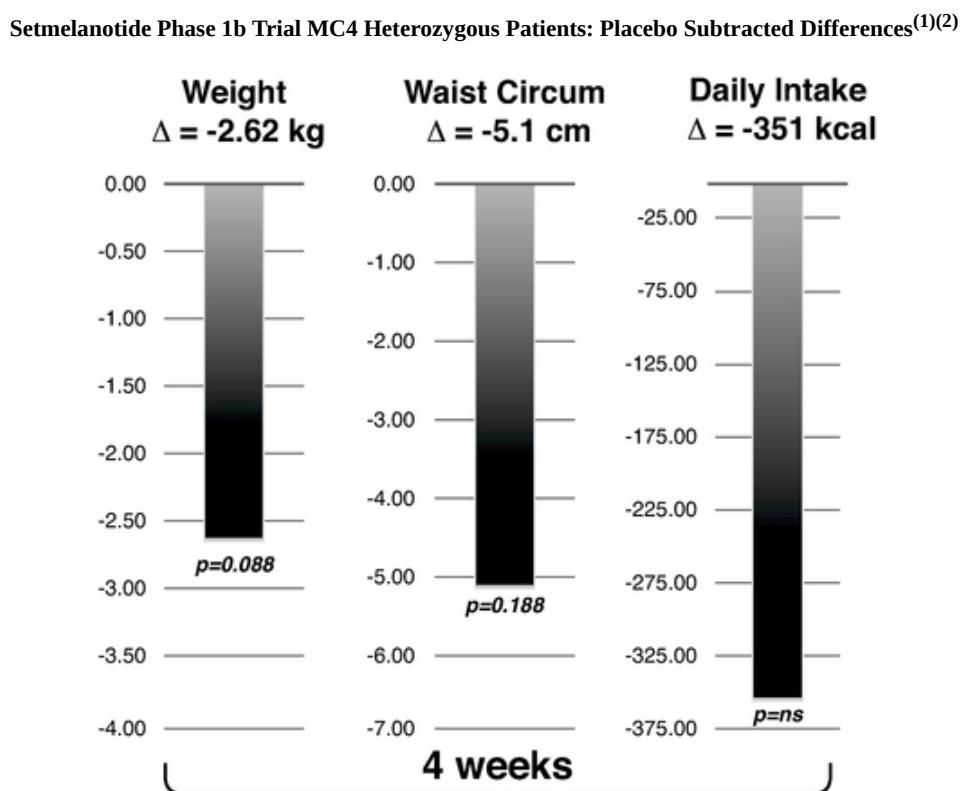
There is convincing evidence that such epigenetic variants are potentially major factors for an increased individual risk to develop obesity later in life, and we hypothesize that the most obese patients in their populations may benefit from treatment with setmelanotide. However, epigenetic variation is likely not the only reason for the development of obesity in this patient group, because these variants are also observed in normal weight individuals, although to a lesser extent. At this point, no epidemiology data is available to estimate the size of the POMC epigenetic deficiency obese population.

We will study patients who are severely obese, or whose BMI is equal to or greater than 40kg/m², and who have hypermethylation at the POMC gene. The purpose of studying these patients in this trial is to provide proof of concept that severely impaired, epigenetic POMC variant obesity patients will also demonstrate significant weight loss similar to, though possibly of less magnitude, as that seen in patients with POMC deficiency obesity or LepR deficiency obesity. We plan to enroll our first patients for this indication in the second half of 2017 at sites in the United States and Europe, and to complete enrollment in 2018. We expect to report preliminary results in the first half of 2018.

Phase 1b Clinical Development in Patients with Heterozygous MC4R Gene Mutations

Early studies in downstream MC4 pathway defects demonstrated good efficacy and tolerability, and served as a foundation for potentially greater efficacy in upstream MC4 pathway deficiencies. We established proof of concept for efficacy of setmelanotide in patients with an MC4R heterozygous genetic mutation in one cohort of patients in our Phase 1b clinical trial. This clinical trial was a double-blind, placebo-controlled, randomized Phase 1b clinical trial designed to evaluate the effect of setmelanotide on weight loss and safety in obese patients with a heterozygous mutation of the MC4R gene. The initial cohort of eight patients was treated for four weeks with setmelanotide or placebo. The setmelanotide group showed weight loss of 3.48 kg, or 7.67 lbs., approximately 2.62 kg, or 5.78 lbs., more weight loss than the placebo group, which showed weight loss of 0.85 kg, or 1.87 lbs. Other parameters supporting weight loss were also positively impacted by setmelanotide. We believe that these results support the hypothesis that setmelanotide can be effective in weight loss in MC4R deficient patients, and provide evidence of the minimum expected treatment effect of setmelanotide, approximately 0.9 kg/week, or 1.98 lbs./week, of weight loss over four weeks, even in a situation where setmelanotide's action is on a downstream MC4 pathway that is no longer fully functional due to heterozygous MC4R mutations. However, our focus is on upstream disorders of the MC4 pathway where we hypothesize that setmelanotide can serve as replacement therapy and provide more compelling efficacy.

The following figure depicts preliminary data relating to our setmelanotide Phase 1b clinical trial in MC4 heterozygous deficiency obesity patients:



(1) Over four weeks of treatment with setmelanotide 0.01 mg/kg/day by continuous SC infusion.

(2) Preliminary data.

In general, we consider a p-value of 0.05 to be significant. P-values are an indication of statistical significance reflecting the probability of an observation occurring due to chance alone. However, it is not possible to determine a p-value for very small sample sizes, such as one- or two-patient trials.

Other Clinical Initiatives in Genetic Obesity

Genotyping Study

Leveraging new understanding of severe obesity caused by specific genetic defects has the potential to improve both diagnosis and treatment for specific types of life-threatening obesity. Therefore, we are sponsoring the Genetic Obesity Project, which is dedicated to improving the understanding of severe obesity that is caused by specific genetic defects—particularly rare genetic disorders that result in life-threatening obesity. As part of that initiative, we have initiated a genotyping study—the Genetic Obesity ID -- Genotyping Study—in which eligible patients are genotyped for rare genetic disorders of obesity. The goal is to develop a screening algorithm for selecting patients to be genotyped and diagnosed with POMC deficiency obesity and LepR deficiency obesity, and to guide further genotyping efforts; in addition, it is our expectation that patients who can participate in our clinical trials will be genetically identified. We are currently including other MC4 pathway deficiencies in the study. Key entry criteria for the study include a history of severe, early onset obesity, along with hyperphagia and are consistent with the recently published Pediatric Obesity guidelines published by the Endocrine Society. Study investigators, who are academic experts in childhood obesity, are located in both the United States and

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Europe. We plan to work with these investigators to publish the results of this study and guidance on the use of the algorithm for screening, to enable more systematic diagnoses of these rare genetic disorders of obesity. Our preliminary results in 560 genotyped patients, described below, suggest we can successfully identify these patients using our algorithms. We intend to validate these early results in larger numbers of patients, but we believe these results provide preliminary support for our genotyping approach.

Number of Patients	Percent	Genetic Defect
2	0.36%	POMC deficiency obesity (PCSK1)
3	0.54%	LepR deficiency obesity
59	10.5%	Heterozygous deficiency
5	0.89%	R236G Heterozygous deficiency

Genetic Epidemiology Studies

We have estimated the patient population for our rare genetic disorders of obesity primarily by identifying patients or by estimating from clinical epidemiology information. Another method to estimate the size of these ultra-rare populations is by genetic epidemiology—using newly available large genomic databases, both full genome sequencing or exome sequencing, that are now becoming available. We have begun some substantial efforts with a series of such databases and/or collaborators and much of our preliminary work has been with a database of approximately 140,000 genomes, representative of the U.S. population.

While results from this effort are preliminary, they have been very supportive of our clinical epidemiological estimates, even when using conservative assumptions. They support that estimates of the number of patients in the United States who are homozygous deficient in the POMC gene, which is one of the genetic defects causing POMC deficiency obesity, and who are homozygous deficient in the LepR gene are at least as large as our assumptions provided above, if not larger. In addition, the estimates of patients who are homozygous deficient in the PCSK1 gene, which is the other genetic defect causing POMC deficiency obesity, may be substantially larger than our estimates, at more than 1,000 patients in the United States. We have already begun to expand this work into other genomic databases that contain patients with different demographics, and are actively working with a series of academic and industry collaborators. The ongoing expansion of genomic data available in other forums also has the effect of supporting this effort. An important improvement in this effort will be working with data linked to phenotypic information to better characterize the genetic information we are analyzing. However, until these data are confirmed in additional genetic epidemiology databases, we must continue to base our patient population estimates on clinical epidemiological information.

Setmelanotide: Clinical Development Program in Prader-Willi Syndrome

PWS is a life threatening, orphan multigenic disease with prevalence estimates ranging from approximately one in 8,000 to one in 52,000, with at least 8,000 diagnosed patients in the United States. A hallmark of PWS is hyperphagia, leading to severe obesity and other complications. For PWS patients, hyperphagia and obesity are the greatest threats to their health, and these patients are likely to die prematurely as a result of choking, stomach rupture, or from complications caused by morbid obesity.

The genetics of PWS are complex, involving many genes on chromosome 15 that are not properly expressed. Recent discoveries highlight that a defect in one of these, the melanoma antigen family L2, or MAGEL2, gene, in rodent models impairs the function of POMC neurons, which are key components of the MC4 pathway. Studies have suggested a link between defects in MAGEL2 in some humans with obesity, hyperphagia, autism spectrum disorders, reduced intellectual ability and most other aspects of behavior and metabolism associated with PWS. However, the connection of PWS with the MC4 pathway is complex.

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We have completed a Phase 2 proof of concept, double-blind, placebo-controlled, randomized clinical trial in PWS, Study RM-493-010, which enrolled 40 patients for four weeks of active setmelanotide treatment, administered once daily by SC injection. This trial was intended to assess the effects of setmelanotide on weight reduction, and PWS-specific hyperphagia-related behaviors, as PWS patients do not respond to hunger questionnaires, as well as determine its safety profile. Based on the data from this Phase 2 clinical trial, we do not believe we will be positioned to proceed directly into a Phase 3 clinical trial.

The trial included a two-week run-in period, a four-week double blind, randomized, placebo-controlled parallel group main trial, a two-week double-blind, randomized, placebo-controlled withdrawal period during which half of the trial patients were randomized to either continue to receive their therapy or be switched to the alternative therapy, from active to placebo, or vice versa, and a two-week active-treatment extension. There were four treatment arms in the trial: placebo (N=14); 0.5 mg of setmelanotide SC injection daily (N=4), 1.5 mg of setmelanotide SC injection daily (N=12), and 2.5 mg of setmelanotide SC injection daily (N=10). Patients were 17 to 54 years of age, with a mean BMI of 39.4 kg/m^2 , and with a genetically confirmed diagnosis of PWS. Primary endpoints for the trial included safety and tolerability, weight loss and hyperphagia, with hyperphagia to be measured by a PWS hyperphagia observer reported outcome, or ORO, questionnaire. Secondary endpoints included dual-energy x-ray absorptiometry measurements, pharmacokinetics, effects during the randomized withdrawal stage, and effects on quality of life and food-related and other behaviors. Primary evaluations were assessed at the end of the four-week double blind parallel group stage, as well as after the withdrawal stage and open label extension.

The results of the trial showed modest effects on hyperphagia, which did not approach statistical significance, and no effect on weight, though there may have been some small evidence of clinically-important weight loss in the very small group of patients who were randomized to the highest dose of setmelanotide over the longest interval of treatment (N=4 patients, post-hoc evaluation, non-significant). There was good safety and tolerability, providing support for the 2.5 mg daily dose, with only injection site reactions common in both active and placebo groups. There were no serious adverse events, no significant safety issues or changes in labs or other safety parameters, and the one discontinuation was due to injection site reactions.

PWS is a complex multigenic disease, and the hypothesis that PWS is an upstream MC4 pathway disorder is supported primarily on the role of only one of those genes, MAGEL2, in animal models of obesity. Our results may support that PWS is not an upstream MC4 pathway disorder. Alternatively, other design factors may have influenced the outcome of this trial, and we will reassess in 2018 the possibility of future Phase 2 trials in PWS that address these potential factors: longer duration of treatment, younger patient population, improved setmelanotide pharmacokinetics, consideration of higher doses, and operational limitations of the completed Phase 2 trial.

Setmelanotide Clinical Development in General Obesity Patients

Initial studies in general obesity provided preliminary evidence of efficacy and of good tolerability, and served as a foundation for the clinical development of setmelanotide. The general obese population is defined as having a BMI of equal to or greater than 30 kg/m^2 . In our initial clinical trials, we delivered setmelanotide with continuous SC infusion using an insulin pump. More recently, our administration has been converted to a once daily SC injectable formulation. In addition, we have an ongoing trial to assess the pharmacokinetics of a new, long-acting formulation of setmelanotide.

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The table below summarizes the setmelanotide studies that we conducted in general obese patients under IND # 112595 submitted to the Division of Metabolism and Endocrinology Products, Center for Drug Evaluation and Research, FDA.

Completed and Ongoing Setmelanotide Clinical Trials in the General Obese Population

Short Study Title	Population	Route of Administration Formulation	Number of Subjects/ Patients	Status
RM-493-001 Single Ascending Dose Trial in Healthy Obese Subjects	Obesity	Continuous infusion	36 healthy obese subjects	Completed
RM-493-002 Multiple Ascending Dose Trial in Healthy Obese Subjects	Obesity	Continuous infusion SC injection	54 healthy obese subjects	Completed
RM-493-003 A Phase 2a Weight Loss Trial in Obese Patients using Continuous Infusion	Obesity	Continuous infusion	74 healthy obese subjects	Completed
RM-493-005 Pre-screening Genetic Testing of Healthy Obese Subjects	N/A Genetic Screening Study	N/A	N/A	Completed
RM-493-006 A Phase 1b 2-Period Crossover Trial on Energy Expenditure in Obese Subjects	Energy Expenditure In Obesity	Continuous infusion	12 healthy obese subjects	Completed
RM-493-008 A Phase 1 Pharmacokinetic Trial of New Once-daily Injectable Formulations	PK/Obesity	SC injection	12 healthy obese subjects	Completed
RM-493-009 A Staged, Phase 1b/Phase 2a Pharmacokinetic/Weight Loss Trial in Obese Patients using Sub-Cutaneous Injection	Obesity	SC injection	97 healthy obese subjects	Completed
RM 493 017 A Long-Acting Formulation PK Study of RM-493	Obesity	SC injection of long-acting formulation	30 healthy obese subjects	Ongoing

SC=subcutaneous.

Phase 2 Clinical Development in the General Obese Population

a. Phase 2 Clinical Trial Results with Continuous Infusion

We conducted our first Phase 2 clinical trial of setmelanotide using continuous SC infusion. This was a 12-week, Phase 2 proof of concept clinical trial in general obese patients using the SC continuous infusion formulation of setmelanotide delivered by an insulin pump. We treated approximately 74 obese patients with either placebo or setmelanotide at a dose of 1.0 mg over

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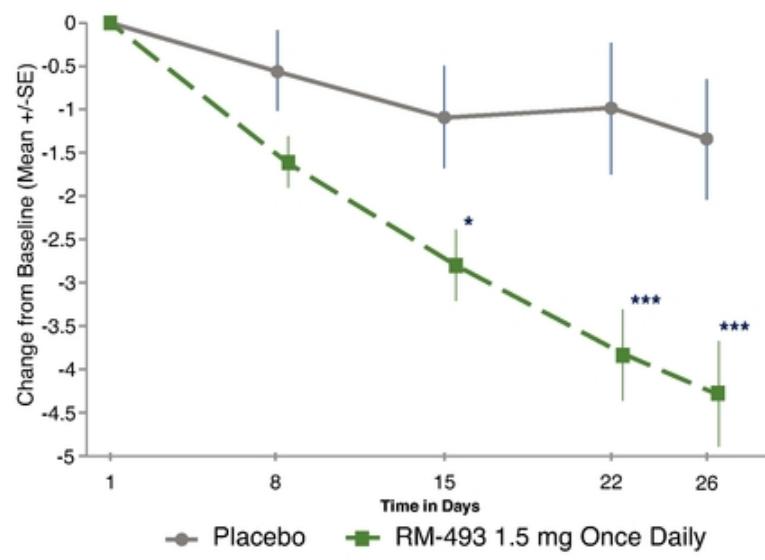
24 hours, with no serious adverse events or other safety indications from laboratory tests, electrocardiograms or vital signs noted in the setmelanotide treatment group. Evaluation of the pharmacokinetics, or blood levels, of setmelanotide from this clinical trial demonstrated that the SC continuous infusion method of drug administration was not optimal. A large number of patients did not meet the target pharmacokinetic exposures of setmelanotide that our Phase 1 clinical trials suggested would have to be achieved in order for setmelanotide to show efficacy. This clinical trial did not demonstrate statistically significant weight loss compared to the placebo. We believe patients in this clinical trial lacked adequate exposure to setmelanotide, and concluded that all future efficacy clinical trials in obese patients should be conducted using the SC injection method. This belief is based on a prior Phase 1 pharmacokinetic trial, which used the SC injection formulation and demonstrated higher pharmacokinetic exposures in obese patients.

b. Phase 2 Clinical Trial with Once Daily SC Injection

We conducted a three-stage, randomized, placebo-controlled, Phase 2 12-week general obesity trial, with approximately 100 obese patients, using our SC injection formulation, primarily with once daily dosing. We designed this Phase 2 clinical trial to bridge between the earlier clinical trials that used continuous infusion and all future clinical trials that use the formulation for once daily SC injection. Therefore, the primary purpose of the staged approach in this trial was to assess if appropriate pharmacokinetic targets could be reached with the new SC injection, first in an in-patient setting similar to the setting where robust weight loss was demonstrated in the Phase 1 general obesity trial, and then in an outpatient setting.

Overall, setmelanotide demonstrated significant weight loss over 12-weeks in all stages, with placebo subtracted weight loss, or the difference in the amount of weight gained or lost in the active treatment group as compared to the placebo treatment group, from baseline of -2.78% to -4.69% and p-values ranging from 0.005 to <0.001. However, weight loss was more pronounced and consistent in the cohort treated with an initial four-week, observed dosing, inpatient period, for which overall placebo subtracted weight loss from baseline at week 12 ranged from -3.87% to -4.69%, all with p-values of less than 0.005, with the most pronounced weight loss during the in-patient period. The once daily SC injection formulation also showed consistent and predictable pharmacokinetic measurements during the four-week inpatient interval in the first stage, validating the characteristics of the SC injection formulation. However, this trial demonstrated challenges in drug administration and compliance when administered in an outpatient setting in the general obese population.

Setmelanotide Phase 2 SC Injection Trial 4-week In-Patient Dosing Period: Percent Weight Loss for Setmelanotide 1.5 mg/day SC injection vs Placebo over 26 days of Observed Dosing



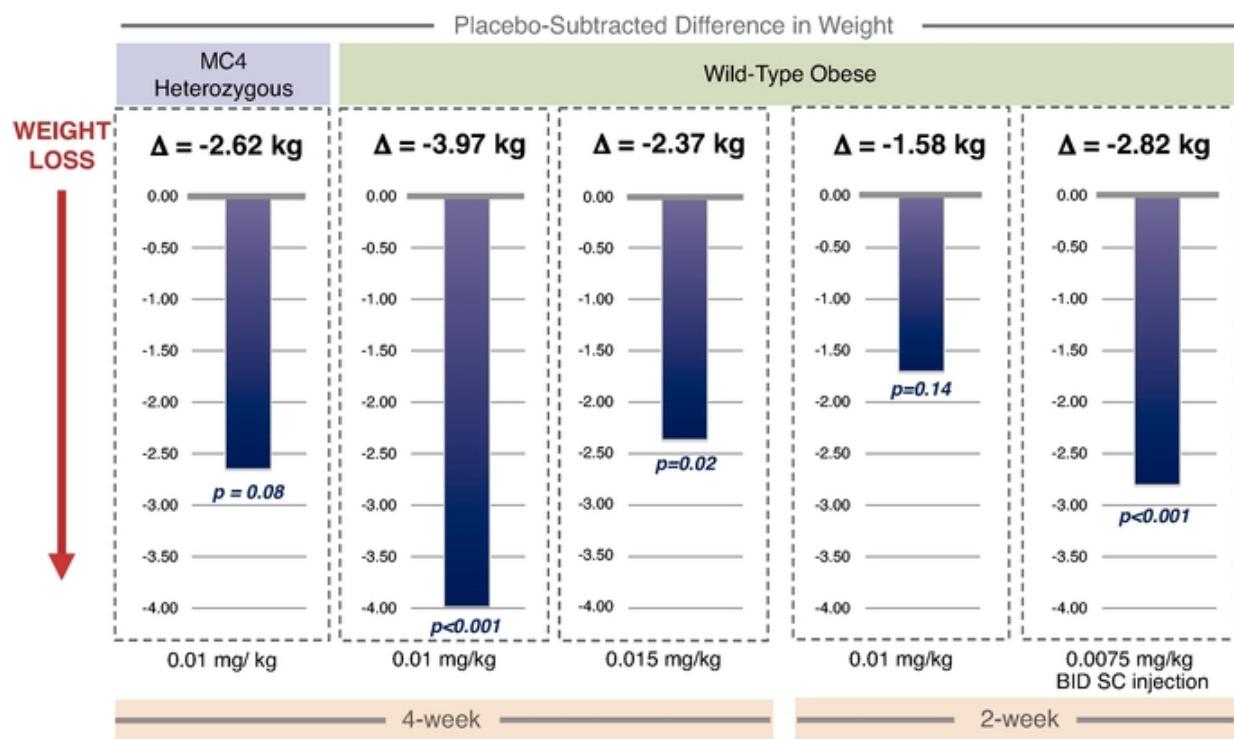
Phase 1 Clinical Development in the General Obese Population

We have completed a Phase 1 single-ascending dose, or SAD, clinical trial of setmelanotide, as well as five cohorts in a Phase 1 multiple-ascending dose, or MAD, clinical trial of setmelanotide. Both clinical trials were in healthy obese subjects, and included a double-blind, placebo-controlled randomized escalating dose design. Subjects received treatment in these Phase 1 clinical trials for one day at doses up to 0.1 mg/kg/day, which is a total daily dose of approximately 10 mg/day, and for up to 28 days at doses up to 0.015 mg/kg/day, which is a total daily dose of approximately 1.5 mg/day.

In the SAD clinical trial, our extensive monitoring of heart rate and blood pressure did not demonstrate any clinically meaningful changes with setmelanotide treatment compared with placebo. Similarly, in the MAD clinical trial, there was no evidence of any notable changes in cardiovascular parameters compared to placebo when assessed by 24-hour ambulatory blood pressure monitoring, or ABPM. We determined that the terminal half-life of setmelanotide is approximately nine to ten hours, making it suitable for once daily dosing.

Four cohorts of the Phase 1 MAD clinical trial that included doses of greater than 0.01 mg/kg/day, which is approximately 1 mg/day, for two to four weeks, demonstrated placebo subtracted weight loss differences. Most panels showed statistically significant, placebo subtracted weight reduction that ranged from 0.6 to 1.4 kg/week, with a mean of approximately 0.9 kg/week over the two to four weeks of treatment in Phase 1.

Setmelanotide: Phase 1b General Obesity Patients: Placebo Subtracted Differences⁽¹⁾⁽²⁾



(1) Over two to four weeks of treatment with setmelanotide by continuous SC infusion. Placebo subtracted differences are the FDA's primary weight loss analysis approach, assessing the weight difference between active and placebo treatment groups for changes from baseline for weight.

(2) Preliminary data.

D = Placebo subtracted weight loss from baseline.

BID = Two times per day.

Phase 1 Energy Expenditure Clinical Trial

In collaboration with the National Institute of Diabetes, Digestive and Kidney Diseases, we investigated setmelanotide in a Phase 1 clinical trial to determine the effects of setmelanotide on energy expenditure, a mechanism for weight loss, in addition to the well-known effects of MC4R agonists on appetite and food intake. Twelve obese adults were randomized to receive setmelanotide or placebo by continuous SC infusion over 72 hours, followed immediately by crossover to the other treatment. Setmelanotide showed statistically significant 6.85% increases in resting energy expenditure, supporting a role for setmelanotide in weight regulation. This trial provided the first clinical demonstration that MC4R activation with setmelanotide increases resting energy expenditure in obese humans.

Long-Acting Setmelanotide Pharmacokinetic Trial

In addition to developing the once daily SC injectable formulation of setmelanotide that we are using in our ongoing clinical trials, in collaboration with Camurus AB, or Camurus, we have developed a once weekly, long-acting formulation using FluidCrystal® technology. When injected subcutaneously, aqueous body fluid is absorbed by the excipient lipid phase which forms a gel-like depot consisting of liquid crystals formed in situ leading to slow diffusion of setmelanotide from the depot.

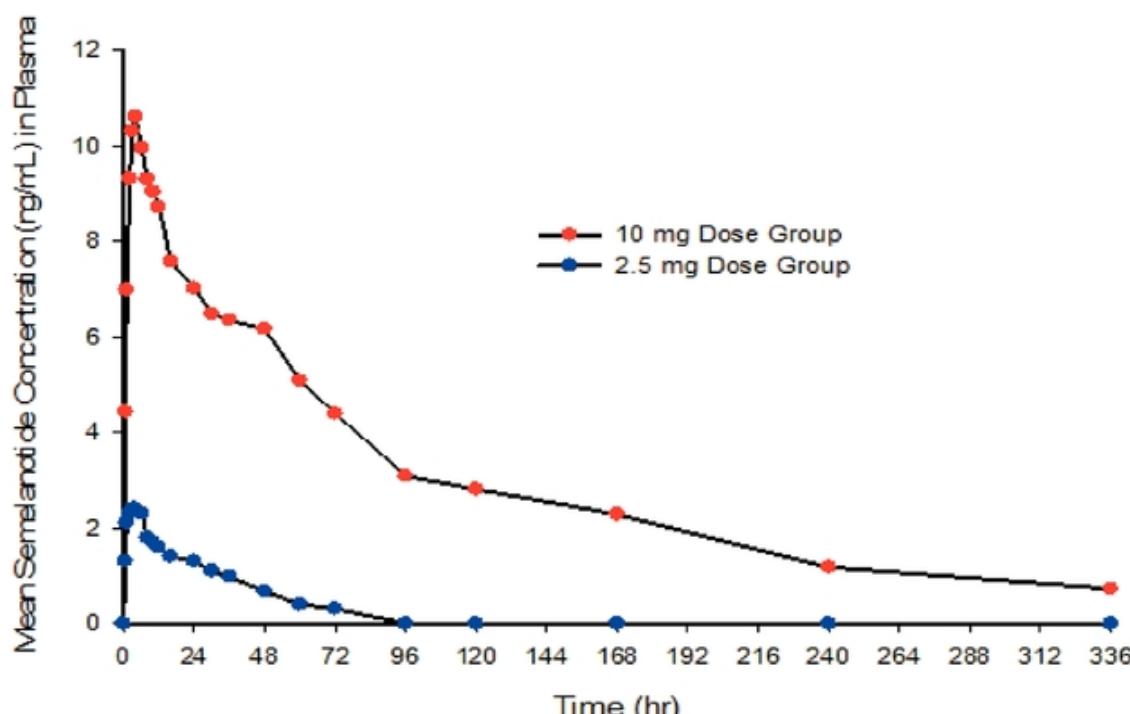
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We have compelling preclinical data with the long-acting formulation: in monkeys, the terminal half-life of the long-acting formulation is approximately 105 hours, and in rats, approximately 92 hours. Two-week toxicology studies in rats have been completed, and the long-acting formulation was well tolerated. During the two-week dosing period, animals given setmelanotide had dose-related, statistically significant lower body weights, from -9.8% to -11.7%, compared to those given placebo controls. Food consumption for animals given setmelanotide was also lower compared to controls, which decreased by approximately -20.5%.

A clinical pharmacokinetic trial is ongoing. It is an ascending-dose, placebo-controlled, up to three sequential panel PK trial, and PK and safety/tolerability will be collected for approximately 14 days. Dose for the three panels will range from 2.5 mg up to 30 mg given as a single SC injection.

The results from the 2.5 mg and 10 mg doses are now available. At these doses, setmelanotide long-acting formulation was well tolerated. The pharmacokinetic data from the 10 mg single subcutaneous dose showed a profile that was consistent with once weekly dosing with a mean pharmacokinetic half-life of 123 hours. While this data is preliminary, and this formulation is expected to be only ready for submission in 2019, or later, this simpler dosing regimen may provide improvements in patient convenience.

Mean Setmelanotide Concentrations (ng/mL) After a Single Subcutaneous Dose of the Long-Acting Camurus Formulation of Setmelanotide in Healthy Obese Subjects (N=8)



Safety and Tolerability

Historically, clinical data with other MC4R therapies suggested that MC4R-mediated side effects may include changes in blood pressure and heart rate, increased erections in males, changes in libido and sexual function in females and nausea and vomiting. As a result, primarily due to concerns about blood pressure and heart rate changes, none of these therapies have proceeded to commercialization and no other MC4R agonists are currently in the clinic for the treatment of obesity and/or hyperphagia. It is noteworthy that the pattern of effects differed among each of the other MC4R therapies, underscoring the complex physiology of MC4R. With setmelanotide, there has been little, if any, evidence of blood pressure or heart rate

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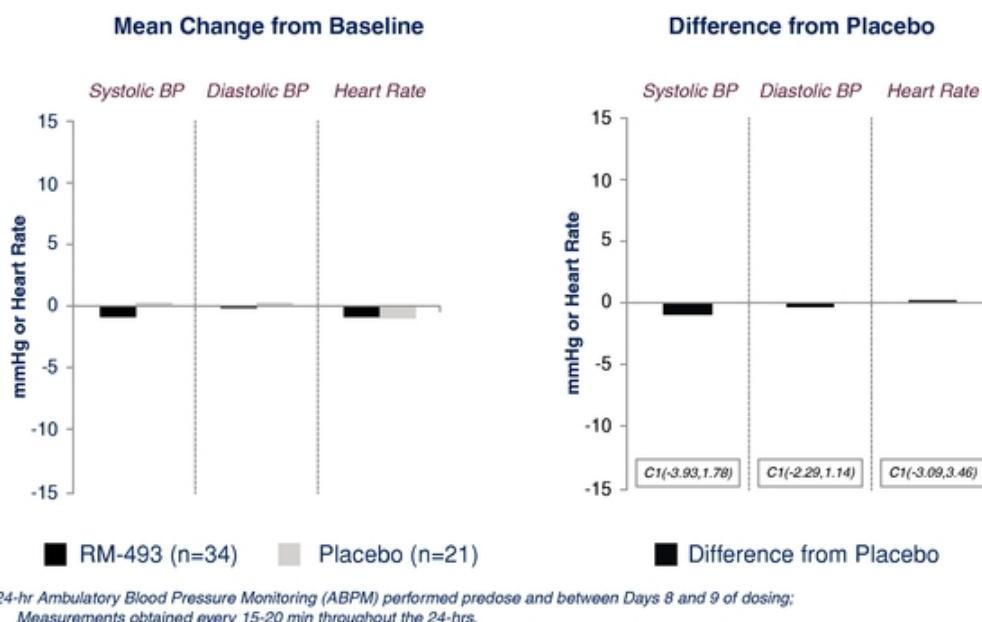
changes, preliminarily supporting an important differentiation of setmelanotide from previous MC4R therapies. Careful monitoring for blood pressure and heart rate changes, as well as other potential adverse events, is included in all setmelanotide clinical trials.

Because of these first generation MC4 therapy failures, the setmelanotide program employed an intensive preclinical screening program to assess clinical candidates for blood pressure and heart rate effects, along with efficacy. The cornerstone of this preclinical screening program was a significant investment in obese primate studies which validated setmelanotide as a promising compound for clinical development.

Setmelanotide was generally well tolerated in our Phase 1 and Phase 2 clinical trials. Overall, except as outlined below, the number and patterns of adverse events was generally low, and the intensity of the adverse events was generally mild, and infrequently led to clinical trial discontinuation.

There has been only a single serious adverse event possibly attributed to setmelanotide in our clinical trials. In our Phase 2 clinical trial with once daily SC injection, one patient was hospitalized for unusual chest pain, but no evidence of any serious respiratory or cardiac cause was found after careful evaluation, and the event was attributed to musculoskeletal pain. There were no treatment-related changes in physical examination, except as noted below, and few, if any, clinically relevant changes in electrocardiograms, laboratory data and/or anti-drug antibodies. Overall, there have been five other serious adverse events in the full development program, in addition to the serious adverse event described above: two others on setmelanotide, including left arm numbness and influenza immunization reaction, and three on placebo consisting of biliary dyskinesia, severe groin strain, and pelvic inflammatory disease. None of these five other serious experiences was considered related to setmelanotide treatment.

To demonstrate that setmelanotide has the potential to provide a safe cardiovascular profile, we extensively validated setmelanotide in obese primate preclinical studies, with special attention to cardiovascular effects. The results of these studies supported testing in clinical trials. In the clinical trials, we monitored blood pressure and heart rate extensively, primarily by 24-hour ABPM. In most clinical trials, there were multiple 24-hour ABPM periods, both on a pre-treatment and post-treatment basis. Trial-by-trial review of the 24-hour ABPM data shows little, if any, evidence of changes in heart rate and/or blood pressure even at the highest doses tested in Phase 1 and Phase 2 clinical trials. We have also conducted an analysis of 24-hour ABPMs that were obtained pre-dose and post-dose across completed studies, which was presented at the Obesity Society in 2015. This included 128 patients, of which 79 were active and 49 were on a placebo. Overall, there was little, if any, evidence of blood pressure or heart rate changes evident from baseline versus placebo in any trial, preliminarily supporting an important differentiation of setmelanotide from previous MC4 therapies. While the preliminary data are encouraging, there will be continued focus on potential cardiovascular risk until addressed in larger and longer clinical trials.

**Setmelanotide Phase 2 SC Injection Trial: 24-hr ABPM (All Studied Patients),
Showing No Adverse Effect of Setmelanotide on Blood Pressure or Heart Rate**

24-hr Ambulatory Blood Pressure Monitoring (ABPM) performed predose and between Days 8 and 9 of dosing;
Measurements obtained every 15-20 min throughout the 24-hrs.

In the majority of our trials, there was a small increase in penile erections in male patients, as well as signs of sexual arousal in a small number of female patients. These symptoms were infrequent, generally mild, not painful, and short-lived. Most often these symptoms were reported in the first week of treatment. There was a small incidence of nausea and vomiting, as well as injection site reactions, both of which usually were reported as mild, early in treatment, and short-lived. A small number of patients had dose reductions and/or discontinued treatment due to nausea and vomiting.

We also noted darkening of skin and skin lesions, such as moles and freckles, in most patients who received setmelanotide. This was likely caused by activation of the closely related MC1 receptor, the receptor that mediates skin darkening in response to sun exposure. This was observed generally after one to two weeks of treatment, most often plateaued by two to four weeks of treatment, and like sun-related tanning, generally returned to baseline after cessation of exposure.

Other effects, specifically back pain, headaches, fatigue, diarrhea and arthralgia, have been numerically more frequent in setmelanotide-treated patients as compared to placebo patients, but most investigators reported these effects to be unrelated to setmelanotide.

While general obese patients are not currently the focus of setmelanotide studies, the FDA and EMA consider the risk and benefit information observed to date with setmelanotide in general obese patients to be supportive of the continued development of this therapy. These data from general obese patients do not raise any new safety concerns and suggest that substantial benefit, as evidenced by weight loss, is possible.

Preclinical Development

Preclinical studies demonstrated the efficacy of setmelanotide in suppressing food intake and body weight gain in diet-induced obese mice, rats, dogs, and rhesus macaques, as well as in genetic models of obesity, including leptin-deficient ob/ob mice and obese Zucker, or fa/fa (leptin-receptor deficient), rats. Furthermore, setmelanotide is associated with restoring insulin sensitivity in nonclinical models of obesity in rodents and lowering of plasma triglycerides, cholesterol, and free fatty acids.

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In particular, we demonstrated activity in obese non-human primates, where approximately 13% weight loss was demonstrated with eight weeks of treatment, without evidence of cardiovascular toxicity. We also studied obese primates in crossover studies to confirm the lack of cardiovascular toxicity by setmelanotide in obese primates. These preclinical studies also confirmed the cardiovascular effects of previous MC4 therapies that had produced cardiovascular toxicity in humans. In contrast, setmelanotide was without cardiovascular effects in head-to-head studies.

Lastly, the toxicology program to support the NDA filing of setmelanotide for POMC deficiency obesity is near completion. We completed three-month toxicology studies in rats and monkeys, with doses and exposures that are more than 300-fold greater than those at the anticipated clinical doses without evidence of clinically relevant toxicological findings. Similarly, we have also completed chronic toxicity studies (6-month rat, 9-month monkey), which in rats provided 219- (maximum concentration) and 106-times (area under the curve), respectively, and in monkeys 282- and 82-times, respectively, the exposures at the anticipated clinical doses compared to the No-Observed-Adverse-Effect-Level(s) in animals. We have evaluated the potential reproductive and development effects of setmelanotide in rats and rabbits with administration by SC injection, to support the administration of setmelanotide in women of child-bearing potential. In addition, a juvenile toxicology study has been completed that will support dosing in pediatric patients less than 12 years of age. In addition, we are planning carcinogenicity studies, the longest of which is expected to be two years. We believe that the FDA and EMA have each provided preliminary guidance that we may file our initial POMC deficiency obesity NDA and marketing authorization application, respectively, without the carcinogenicity studies for these rare disease populations, which we will then provide post-approval.

Competition

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We have competitors in a number of jurisdictions, many of which have substantially greater name recognition, commercial infrastructures and financial, technical and personnel resources than we have. Established competitors may invest heavily to quickly discover and develop compounds that could make setmelanotide obsolete or uneconomical. Any new product that competes with an approved product may need to demonstrate compelling advantages in efficacy, convenience, tolerability and safety to be commercially successful. Other competitive factors, including generic competition, could force us to lower prices or could result in reduced sales. In addition, new products developed by others could emerge as competitors to setmelanotide. If we are not able to compete effectively against our current and future competitors, our business will not grow and our financial condition and operations will suffer.

There are no current pharmacological treatments for regulating hunger and hyperphagia-related behaviors of patients with POMC deficiency obesity, LepR deficiency obesity, Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity or POMC epigenetic disorders. Bariatric surgery is not a treatment option for these genetic disorders of obesity because the severe obesity and hyperphagia associated with these disorders are considered to be risk factors for bariatric surgery.

Licensing Agreements

Ipsen Pharma S.A.S.

In February 2010, the Predecessor Company entered into a license agreement with Ipsen S.A.S., or Ipsen, pursuant to which Ipsen granted to it an exclusive, sublicensable, worldwide license to certain patents and other intellectual property rights to research, develop, and commercialize compounds that were discovered or researched by Ipsen in the course of conducting its MC4 program or that otherwise were covered by the licensed patents. Rights under the license included the right to research, develop and commercialize setmelanotide. Pursuant to the license, Ipsen also granted to the Predecessor Company a

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non-exclusive, sublicensable, worldwide license to certain patents and other intellectual property rights that were licensed by Ipsen from a third party or that Ipsen may develop in the future to research, develop, and commercialize any of the compounds exclusively licensed by Ipsen pursuant to the license.

On March 21, 2013, the LLC entity completed the Corporate Reorganization pursuant to which, among other things, the existing license with Ipsen with respect to the MC4 program is now held separately by us. As a result we hold the rights to the MC4 program, including the rights to develop and commercialize setmelanotide.

Under the terms of the Ipsen license agreement, Ipsen will receive payments of up to \$40.0 million upon the achievement of certain development and commercial milestones in connection with the development, regulatory approval and commercialization of applicable licensed products, and royalties on future sales of the licensed products. Substantially all of the aggregate payments under the Ipsen license agreement are for milestones that may be achieved no earlier than first commercial sale of the applicable licensed product. Royalties in the mid-single digits on future sales of the applicable licensed products will be due under the Ipsen license agreement on a licensed product-by-licensed product and country-by-country basis until the later of the date when sales of a licensed product in a particular country are no longer covered by patent rights licensed pursuant to the Ipsen license agreement and the tenth anniversary of the date of the first commercial sale of the applicable licensed product in the applicable country. The term of the Ipsen license agreement continues until the expiration of the applicable royalty term on a country-by-country and product-by-product basis. Upon expiration of the term of the agreement, the licensed rights granted to us under the agreement, to the extent they remain in effect at the time of expiration, will thereafter become irrevocable, perpetual and fully paid-up licenses that survive the expiration of the term. We have a right to terminate the license agreement at any time during the term for any reason on 180 days' written notice to Ipsen. Ipsen has a right to terminate the agreement prior to expiration of its term for our material breach of the agreement, our failure to initiate or complete development of a licensed product or our bringing an action seeking to have an Ipsen license patent right declared invalid. Upon any early termination of the license agreement not due to Ipsen's material breach, all licensed rights granted under the license agreement will terminate.

Camurus

In January 2016, we entered into a license agreement for the use of Camurus' drug delivery technology, FluidCrystal, to formulate setmelanotide with Camurus. Under the terms of the agreement, Camurus granted us a worldwide license to the FluidCrystal technology to formulate setmelanotide and to develop, manufacture, and commercialize this new formulation for once-weekly dosing, administered as a SC injection. The license granted to us is specific to the FluidCrystal technology incorporating setmelanotide. Under the terms of the license agreement, we are responsible for manufacturing, development, and commercialization of the setmelanotide FluidCrystal formulation worldwide. Camurus received a non-refundable and non-creditable upfront payment of \$500,000 in January 2016, and is eligible to receive progressive payments of approximately \$65.0 million, of which the majority are sales milestones. In addition, Camurus is eligible to receive tiered, mid to mid-high, single digit royalties on future sales of the product.

The term of the agreement continues until the expiration of the applicable royalty term on a country-by-country and product-by-product basis. Upon expiration of the term of the agreement, the licensed rights granted to us under the agreement, to the extent they remain in effect at the time of expiration, will thereafter become irrevocable, perpetual and fully paid-up licenses that survive the expiration of the term. We have a right to terminate the license agreement at any time during the term for any reason upon 90 days' written notice to Camurus. Camurus has a right to terminate the agreement prior to expiration of its term for our material breach of the agreement, if we voluntarily or involuntarily file for bankruptcy, or for our bringing an action seeking to have a Camurus license patent right declared invalid.

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Upon any early termination of the license agreement not due to Camurus' material breach, all licensed rights granted under the license agreement will terminate.

Commercial Operations

Our commercial strategies center around creating a well-informed, supportive genetic obesity community of institutions, healthcare providers, patients, caregivers, and payers to support our ongoing research and development efforts to transform the care of patients with MC4 pathway deficiencies.

Our commercial priorities for the launch of setmelanotide include:

- Improving methods of evaluation and diagnosis of rare genetic obesity patients through enhanced diagnostic capabilities and partnership with key opinion leaders and pediatric endocrinologists in order to more clearly articulate the clinical presentation of these patients to referring physicians;
- Facilitating an integrated genetic obesity community through services that support patient awareness, education, advocacy, and treatment;
- Communicating the burden of rare genetic obesity syndromes to promote advocacy for patient sequencing and support for pricing and reimbursement of setmelanotide; and
- Building a global commercial organization to drive patient identification and enable a successful launch of setmelanotide.

Our management team understands the complexity of rare diseases and we believe has the necessary expertise to be a true partner to patients, caregivers, advocacy, and healthcare teams leading to shared success. We intend to establish a specialty sales force and develop an organizational infrastructure that will support an extensive network of endocrinologists and other physicians treating severe childhood obesity and rare genetic disorders of obesity which in turn we believe will help establish genetic obesity centers of excellence. Our goal is for our field personnel to work directly with patients, caregivers and healthcare providers to facilitate therapy initiation and adherence. We also expect to partner with existing and new advocacy organizations to further educate our patient population on genetic obesity and support coverage for setmelanotide. In addition, we intend to establish our own commercial sales and marketing organization in the United States and core strategic markets and to selectively establish partnerships in markets outside the United States for sales, marketing and distribution.

Patents and Proprietary Rights

We have in-licensed a large patent portfolio from Ipsen for our melanocortin programs. The portfolio includes multiple patent families, and all of these in-licensed patent families are being prosecuted or maintained by Ipsen in consultation with us. We have also filed patent applications in four families which are exclusively owned and maintained by us that relate to the melanocortin program.

Our MC4 portfolio of licensed and exclusively owned patent families, which includes setmelanotide, consists of 9 patent families currently being prosecuted or maintained, which include applications and patents directed to compositions of matter, formulations and methods of treatment using setmelanotide. As of May 10, 2017, the portfolio licensed for the MC-4 program consists of seven issued United States patents and 42 issued non-United States patents across four of the 9 families. We are actively pursuing six United States patent applications and 48 non-United States applications in 18 jurisdictions.

In the patent family directed to the composition of matter for setmelanotide, we have two issued United States patents and 21 issued non-United States patents, including Australia, Canada, China, Europe, Hong Kong, Israel, Japan, Korea, New Zealand, Russia and Singapore. The standard 20-year term for patents in this family would expire in 2026, but the United States patent will expire in 2027 due to a patent term adjustment. Patent term extensions for delays in marketing approval may also extend the terms of patents in this family.

In addition to the patents and patent applications discussed above, we have filed one application co-owned with Charité-Universitätsmedizin Berlin, that relates to the melanocortin program, which has not yet entered active prosecution.

Intellectual Property Protection Strategy

We currently seek, and intend to continue seeking, patent protection whenever commercially reasonable for any patentable aspects of setmelanotide and related technology or any new products or product candidates we acquire in the future. Where our intellectual property is not protected by patents, we may seek to protect it through other means, including maintenance of trade secrets and careful protection of our proprietary information. Our license from Ipsen for the melanocortin program require Ipsen, subject to certain exceptions and upon consultation with us, to prosecute and maintain its patent rights as they relate to the licensed compounds and methods. If Ipsen decides to cease prosecution or maintenance of any of the licensed patent rights, we have the option to take over prosecution and maintenance of those patents and Ipsen will assign to us all of its rights in such patents. For those patent rights that we own exclusively, we control all prosecution and maintenance activities.

The patent positions of biopharmaceutical companies are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Consequently, we do not know whether the product candidate we in-license will be protectable or remain protected by enforceable patents. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction, and furthermore, we cannot determine whether the claims of any issued patents will provide sufficient proprietary protection to protect us from competitors, or will be challenged, circumvented or invalidated by third parties. Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. This potential issue is exacerbated by the fact that, prior to March 16, 2013, in the United States, the first to make the claimed invention may be entitled to the patent. On March 16, 2013, the United States transitioned to a "first to file" system in which the first inventor to file a patent application may be entitled to the patent. Therefore, we may have to participate in interference proceedings declared by the United States Patent and Trademark Office, or PTO, or a foreign patent office to determine priority of invention. Moreover, we may have to participate in other proceedings declared by the United States PTO or a foreign patent office, such as post-grant proceedings and oppositions, that challenge the validity of a granted patent. Such proceedings could result in substantial cost, even if the eventual outcome is favorable to us.

Although we currently have issued patents directed to a number of different attributes of our products, and pending applications on others, there can be no assurance that any issued patents would be held valid by a court of competent jurisdiction. An adverse outcome could subject us to significant liabilities to third parties, require disputed rights to be licensed from third parties or require us to cease using specific compounds or technology. To the extent prudent, we intend to bring litigation against third parties that we believe are infringing our patents.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the United States PTO in granting a patent, or may be shortened if a patent is terminally disclaimed over another patent with an earlier expiration date.

As mentioned above, in the United States, the patent term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration as

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compensation for the patent term lost during the FDA regulatory review process. In the future, if and when our pharmaceutical products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We intend to seek patent term adjustments and extensions to any of our issued patents in any jurisdiction where these are available, however there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such adjustments or extensions.

To protect our rights to any of our issued patents and proprietary information, we may need to litigate against infringing third parties, or avail ourselves of the courts or participate in hearings to determine the scope and validity of those patents or other proprietary rights. These types of proceedings are often costly and could be very time-consuming to us, and we cannot be certain that the deciding authorities will rule in our favor. An unfavorable decision could result in the invalidation or a limitation in the scope of our patents or forfeiture of the rights associated with our patents or pending patent applications. Any such decision could result in our key technologies not being protectable, allowing third parties to use our technology without being required to pay us licensing fees or may compel us to license needed technologies from third parties to avoid infringing third-party patent and proprietary rights. Such a decision could even result in the invalidation or a limitation in the scope of our patents or could cause us to lose our rights under existing issued patents or not to have rights granted under our pending patent applications.

In addition, we intend to seek orphan drug exclusivity in jurisdictions in which it is available. A prerequisite to orphan drug exclusivity in the United States and in the European Union is orphan drug designation. An orphan drug designation may be granted where a drug is developed specifically to treat a rare or uncommon medical treatment. If a product which has an orphan drug designation subsequently receives the first regulatory approval for the indication for which it has such designation, the product is entitled to orphan exclusivity, meaning that the applicable regulatory authority may not approve any other applications to market the same drug for the same indication, except in certain very limited circumstances, for a period of seven years in the United States and 10 years in the European Union. Orphan drug exclusivity does not prevent competitors from developing or marketing different drugs for an indication.

We also rely on trade secret protection for our confidential and proprietary information. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, no assurance can be given that others will not independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose such technology, or that we can meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual will be our exclusive property. There can be no assurance, however, that these agreements will provide meaningful protection or adequate remedies for our trade secrets in the event of unauthorized use or disclosure of such information.

Manufacturing

We currently contract with a third party for the manufacture of setmelanotide and intend to continue to do so in the future. We have entered into a process development and manufacturing services agreement with CordenPharma International, formerly Peptisyntha SA prior to its acquisition by CordenPharma International, or Peptisyntha, under which Peptisyntha will provide certain process development and manufacturing services in connection with the manufacture of setmelanotide. Under the agreement, we pay Peptisyntha for services in accordance with the terms of mutually agreed upon work orders, which we and Peptisyntha may enter into from time to time. The agreement also provides that, subject to certain conditions, for a period following each product launch date, we will source from Peptisyntha a portion of

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our requirements for that product being sourced from non-affiliate third parties. Under the agreement, each party is subject to customary indemnification provisions.

The Peptisyntha agreement will continue, unless earlier terminated pursuant to its terms, until the later of six years from the July 17, 2013 effective date or the completion of all services under all work plans executed in accordance with the terms of the agreement prior to the sixth anniversary of its effective date. The agreement may be extended by us continuously for additional two-year periods upon written notice to Peptisyntha. We also may terminate the agreement or any work order thereunder upon at least 30 days' prior written notice to Peptisyntha.

We have also entered into a process development and manufacturing services agreement with Recipharm Monts S.A.S., or Recipharm, under which Recipharm will provide certain process development and manufacturing services in connection with the manufacture of setmelanotide. Under the agreement, we pay Recipharm for services in accordance with the terms of mutually agreed upon work orders, which we and Recipharm may enter into from time to time. Under the agreement, each party is subject to customary indemnification provisions. The Recipharm agreement will continue, unless earlier terminated pursuant to its terms, until the later of three years from the December 21, 2016 effective date or the completion of all services under all work plans executed in accordance with the terms of the agreement prior to the third anniversary of its effective date. The agreement may be extended by us continuously for additional two-year periods upon written notice to Recipharm. We also may terminate the agreement or any work order thereunder upon at least 60 days' prior written notice to Recipharm.

Our contract manufacturing agreements give us visibility into the expected future cost of producing setmelanotide at commercial scale. Based upon a range of prices of currently-marketed therapies indicated for orphan diseases, we believe that our cost of goods for setmelanotide will be highly competitive.

We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. To meet our projected needs for clinical supplies to support our activities through regulatory approval and commercial manufacturing, the contract manufacturing organizations, or CMOs, with whom we currently work will need to increase scale of production or we expect that we will need to secure alternate suppliers. We have not currently identified alternate suppliers in the event the current CMOs we utilize are unable to scale production. Because we rely on these CMOs, we have personnel with pharmaceutical development and manufacturing experience who are responsible for maintaining our CMO relationships.

Regulatory Matters

Government Regulation and Product Approvals

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other competent authorities, require the expenditure of substantial time and financial resources.

Review and Approval of Drugs in the United States

In the United States, the FDA approves drug products under the Federal Food, Drug, and Cosmetic Act, or FDCA, and associated implementing regulations. Biological products, on the other hand, are licensed by the FDA under the Public Health Service Act, or PHSA. With passage of the Biologics Price Competition and Innovation Act of 2009, Congress amended the definition of "biological product" in the PHSA so as to exclude a chemically synthesized polypeptide from licensure under the PHSA. Rather, the Act provided that such products would be treated as drugs under the FDCA. Subsequently, through final

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guidance issued in April 2015, the FDA indicated that a "chemically synthesized polypeptide" is any alpha amino acid polymer that is made entirely by chemical synthesis and is less than 100 amino acids in size. Accordingly, based on this FDA guidance, we believe that our products will not be treated as biologics subject to approval of a biologics license application, or BLA, by the FDA, and rather will be treated as drug products subject to approval of a new drug application, or NDA, by the FDA pursuant to the FDCA.

The failure to comply with applicable requirements under the FDCA and other applicable laws at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with current Good Clinical Practices, or cGCPs, to establish the safety and efficacy of the proposed drug product for each proposed indication;
- preparation and submission to the FDA of an NDA requesting marketing for one or more proposed indications;
- review by an FDA advisory committee, where appropriate or if applicable, as may be requested by the FDA to assist with its review;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with cGCPs and the integrity of the clinical data;
- payment of user fees, per published Prescription Drug User Fee Act, or PDUFA, guidelines for the relevant year, and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

Preclinical Studies

Before an applicant begins testing a compound with potential therapeutic value in humans, the drug candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as *in vitro* and animal studies to assess the potential safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP

regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved drug to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug that is not the subject of an approved NDA. In support of a request for an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When the foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements in order to use the study as support for an IND or application for marketing approval. Specifically, on April 28, 2008, the FDA amended its regulations governing the acceptance of foreign clinical studies not conducted under an investigational new drug application as support for an IND or a new drug application. The final rule provides that such studies must be conducted in accordance with good clinical practice, or GCP, including review and approval by an independent ethics committee, or IEC, and informed consent from subjects. The GCP requirements in the final rule encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the

clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its ClinicalTrials.gov website.

Human Clinical Studies in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in the following sequential phases, which may overlap or be combined:

- Phase 1: The drug is initially introduced into healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.
- Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.
- Phase 4: Post-approval studies, which are conducted following initial approval, are typically conducted to gain additional experience and data from treatment of patients in the intended therapeutic indication.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected

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serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

During the course of clinical development the sponsor often refines the indication and endpoints on which the NDA will be based. For endpoints based on PROs and OROs, the process typically is an iterative one. The FDA has issued guidance on the framework it uses to evaluate PRO instruments, and it may offer advice on optimizing PRO and ORO instruments during the clinical development process, but the FDA usually reserves final judgment until it reviews the NDA.

Concurrent with clinical trials, companies often complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality, purity and potency of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

In a general guidance meeting with FDA review staff in 2013, following the opening of our independent new drug application for the development of setmelanotide, the FDA provided us with general principles to follow in designing clinical studies for drugs intended for use in an indication targeted to a specific obese population. In 2015, we received further guidance from FDA review staff in a meeting to discuss clinical endpoints and trial design strategies for the study of setmelanotide in patients with rare genetic forms of obesity. At that meeting, the FDA noted its experience in applying regulatory flexibility for drugs intended to treat rare diseases. It indicated that it would take into account factors related to particular patient populations, such as the prevalence and severity of the disease, but also noted that the requirements for a phase 3 program would depend on the effect observed and the robustness of the results. The FDA also indicated that it would exercise flexibility regarding the timing and requirements for certain preclinical toxicology testing. In 2017, we intend to take advantage of our breakthrough therapy designation by meeting regularly with FDA review staff to discuss methods to shorten the development timeline for an indication in POMC deficiency obesity, and to use the knowledge gained to do likewise for other closely-related indications in rare genetic forms of obesity.

Submission and Review of an NDA by the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to an application user fee, and the sponsor of an approved NDA is also subject to annual product and establishment user fees. For federal fiscal year 2017, the submission of an NDA is subject to an application user fee of \$2,038,100. The annual product and establishment user fees for fiscal year 2017 are \$97,750 per product and \$512,200 per establishment.

Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for drugs with orphan designation and a waiver for certain small businesses, an exception from the establishment fee when the establishment does not engage in manufacturing the drug during a particular fiscal year and an exception from the product fee for a drug that is the same as another drug approved under an abbreviated pathway. Each category of fees is typically increased annually.

The FDA conducts a preliminary review of an NDA generally within 60 calendar days of its receipt and strives to inform the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be

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resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs. Under that agreement, 90% of applications seeking approval of New Molecular Entities, or NMEs, are meant to be reviewed within ten months from the date on which the FDA accepts the NDA for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date. For applications seeking approval of drugs that are not NMEs, the ten-month and six-month review periods run from the date the FDA receives the application. The review process and the Prescription Drug User Fee Act goal date may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including drug component manufacturing, e.g., active pharmaceutical ingredients, finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with cGCP.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy, Priority Review and Regenerative Advanced Therapy Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation, priority review designation and regenerative advanced therapy designation.

Specifically, the FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and

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the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a Fast Track application does not begin until the last section of the application is submitted. In addition, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, a product may be designated as Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case- by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

With passage of the 21st Century Cures Act, or the Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with the FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the

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therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a drug.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit. Thus, the benefit of accelerated approval derives from the potential to receive approval based on surrogate endpoints sooner than possible for trials with clinical or survival endpoints, rather than deriving from any explicit shortening of the FDA approval timeline, as is the case with priority review.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. As a result, a drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to initiate expedited proceedings to withdraw approval of the drug. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are

continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, suspension of the approval, or complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In the United States, healthcare professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in non-promotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information. If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion, and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, and its implementation regulations, as well as the Drug Supply Chain

Security Act, or DSCSA, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the federal level, and set minimum standards for the regulation of drug distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCSA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme allowing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are "abbreviated" because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, the strength and the conditions of use of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug..."

Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the

date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

Under FDARA, a priority review track will be established for certain generic drugs, requiring the FDA to review a drug application within eight months for a drug that has three or fewer approved drugs listed in the *Orange Book* and is no longer protected by any patent or regulatory exclusivities, or is on the FDA's drug shortage list. The new legislation also authorizes the FDA to expedite review of "competitor generic therapies" or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

505(b)(2) NDAs

As an alternative path to FDA approval for modifications to formulations or uses of products previously approved by the FDA pursuant to an NDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments and permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant. If the 505(b)(2) applicant can establish that reliance on FDA's previous findings of safety and effectiveness is scientifically and legally appropriate, it may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements, including clinical trials, to support the change from the previously approved reference drug. The FDA may then approve the new product candidate for all, or some, of the label indications for which the reference drug has been approved, as well as for any new indication sought by the 505(b)(2) applicant.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the application will not be approved until all the listed patents claiming the referenced product have expired, other than method of use patents involving indications for which the applicant is not seeking approval.

If the ANDA or 505(b)(2) applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA or 505(b)(2) application has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the application until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the applicant. The ANDA or 505(b)(2) application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the branded reference drug has expired.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the FDASIA in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and any other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

In addition, FDARA requires the FDA to meet early in the development process to discuss pediatric study plans with drug sponsors. The legislation requires the FDA to meet with drug sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than 90 days after the FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless and until the FDA promulgates a regulation stating otherwise, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application. With regard to patents, the six-month pediatric exclusivity period will not attach to any patents for which a generic (ANDA or 505(b)(2) NDA) applicant submitted a paragraph IV patent certification, unless the NDA sponsor or patent owner first obtains a court determination that the patent is valid and infringed by a proposed generic product.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition, generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product. A company must request orphan drug designation before submitting an NDA for that drug for that rare disease or condition. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the PDUFA goal dates for the regulatory review and approval process, although it does convey certain advantages, such as tax benefits and exemptions from the PDUFA application fee.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same indication for seven years, except in certain limited circumstances. Orphan drug exclusivity does not block the approval of a different drug for the same rare disease or condition, nor does it block the approval of the same drug for different indications. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated on its orphan product application, it may not be entitled to exclusivity.

Under FDARA, orphan exclusivity will not bar approval of another orphan drug under certain circumstances, including if a subsequent product with the same drug for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously required the FDA to recognize orphan exclusivity regardless of a showing of clinical superiority.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension, also known as patent term restriction, under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. Patent term extension is generally available only for drug products whose active ingredient has not previously been approved by the FDA. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate approval date. Patent term extension cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The United States PTO reviews and approves the application for any patent term extension in consultation with the FDA.

FDA Approval and Regulation of Companion Diagnostics

If safe and effective use of a therapeutic product depends on an *in vitro* diagnostic medical device, then the FDA generally will require approval or clearance of that diagnostic, known as an *in vitro* companion diagnostic device, at the same time that the FDA approves the therapeutic product. In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and *in vitro* companion diagnostic devices. According to the guidance, for novel drugs, an *in vitro* companion diagnostic device and its corresponding therapeutic should be approved or cleared contemporaneously by the FDA for the use indicated in the therapeutic product's labeling.

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If FDA determines that an *in vitro* companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, FDA generally will not approve the therapeutic product or new therapeutic product indication if the *in vitro* companion diagnostic device is not approved or cleared for that indication. Approval or clearance of the *in vitro* companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population.

Under the FDCA, *in vitro* diagnostics, including *in vitro* companion diagnostic devices, are generally regulated as medical devices. In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption applies, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution. The two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and premarket approval, or PMA approval. The FDA has generally required *in vitro* companion diagnostic devices intended to select the patients who will respond to a drug to obtain a PMA for that diagnostic simultaneously with approval of the drug.

The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee, which exceeds \$250,000 for most PMAs. In addition, PMAs for certain devices must generally include the results from extensive preclinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, a PMA application typically requires data regarding analytical and clinical validation studies. As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with the Quality System Regulation, or QSR, which imposes elaborate testing, control, documentation and other quality assurance requirements.

PMA approval is not guaranteed, and the FDA may ultimately respond to a PMA submission with a not approvable determination based on deficiencies in the application and require additional clinical trial or other data that may be expensive and time-consuming to generate and that can substantially delay approval. If the FDA's evaluation of the PMA application is favorable, the FDA typically issues an approvable letter requiring the applicant's agreement to specific conditions, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. The FDA may also determine that additional clinical trials are necessary, in which case the PMA approval may be delayed for several months or years while the trials are conducted and then the data submitted in an amendment to the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the applicant. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution. Once granted, PMA approval may be withdrawn by the FDA if compliance with post approval requirements, conditions of approval or other regulatory standards are not maintained or problems are identified following initial marketing.

After a device is placed on the market, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved.

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Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer's manufacturing processes and those of its suppliers are required to comply with the applicable portions of the QSR, which cover the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the United States.

The 21st Century Cures Act

On December 13, 2016, President Obama signed the Cures Act into law. The Cures Act is designed to modernize and personalize healthcare, spur innovation and research, and streamline the discovery and development of new therapies through increased federal funding of particular programs. It authorizes increased funding for the FDA to spend on innovation projects. The new law also amends the Public Health Service Act to reauthorize and expand funding for the National Institutes of Health. The Act establishes the NIH Innovation Fund to pay for the cost of development and implementation of a strategic plan, early stage investigators and research. It also charges NIH with leading and coordinating expanded pediatric research. Further, the Cures Act directs the Centers for Disease Control and Prevention to expand surveillance of neurological diseases.

With amendments to the FDCA and the Public Health Service Act, or PHSA, Title III of the Cures Act seeks to accelerate the discovery, development, and delivery of new medicines and medical technologies. To that end, and among other provisions, the Cures Act reauthorizes the existing priority review voucher program for certain drugs intended to treat rare pediatric diseases until 2020; creates a new priority review voucher program for drug applications determined to be material national security threat medical countermeasure applications; revises the FDCA to streamline review of combination product applications; requires FDA to evaluate the potential use of "real world evidence" to help support approval of new indications for approved drugs; provides a new "limited population" approval pathway for antibiotic and antifungal drugs intended to treat serious or life-threatening infections; and authorizes FDA to designate a drug as a "regenerative advanced therapy," thereby making it eligible for certain expedited review and approval designations.

On August 3, 2017, Congress passed the FDARA. FDARA reauthorizes the various user fees to facilitate the agency's review and oversight relating to prescription drugs, generic drugs, medical devices, and biosimilars. The legislation also includes several policy riders that will impact an array of issues within the FDA's authority including, among others, pediatric study requirements, orphan drug exclusivity, and the approval process for generic drugs.

Regulation and Procedures Governing Approval of Medicinal Products in the European Union

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of setmelanotide to the extent we choose to sell any setmelanotide outside of the United States. Whether or not we obtain FDA approval for a product, we must obtain approval of a product by equivalent competent authorities in foreign jurisdictions before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country. As in the United States, post-approval regulatory requirements, such as those regarding product manufacture, marketing, or distribution would apply to any product that is approved outside the United States.

The process governing the marketing authorization of medicinal products in the European Union entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety, quality and efficacy of the medicinal product for each proposed therapeutic indication.

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It also requires the submission to the relevant competent authorities of a marketing authorization application, or MAA, and granting of a marketing authorization by these authorities before the product can be marketed and sold in the European Union.

Clinical Trial Approval

The Clinical Trials Directive 2001/20/EC, the Directive 2005/28/EC on Good Clinical Practice, or GCP, and the related national implementing provisions of the individual EU member states govern the system for the approval of clinical trials in the European Union. Under this system, an applicant must obtain prior approval from the competent national authority of the EU member states in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by, among other documents, an investigational medicinal product dossier (the Common Technical Document) with supporting information prescribed by Directive 2001/20/EC, Directive 2005/28/EC, where relevant the implementing national provisions of the individual EU member states and further detailed in applicable guidance documents.

In April 2014, the new Clinical Trials Regulation, (EU) No 536/2014 (Clinical Trials Regulation) was adopted. The Regulation is anticipated to enter into force in 2019. The Clinical Trials Regulation will be directly applicable in all the EU member states, repealing the current Clinical Trials Directive 2001/20/EC. Conduct of all clinical trials performed in the European Union will continue to be bound by currently applicable provisions until the new Clinical Trials Regulation becomes applicable. The extent to which on-going clinical trials will be governed by the Clinical Trials Regulation will depend on when the Clinical Trials Regulation becomes applicable and on the duration of the individual clinical trial. If a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation becomes applicable the Clinical Trials Regulation will at that time begin to apply to the clinical trial.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the European Union. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the "EU portal"; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the competent authorities of all EU member states in which an application for authorization of a clinical trial has been submitted (member states concerned). Part II is assessed separately by each member state concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned EU member state. However, overall related timelines will be defined by the Clinical Trials Regulation.

Marketing Authorization

To obtain a marketing authorization for a product under European Union regulatory systems, an applicant must submit an MAA either under a centralized procedure administered by the European Medicines Agency, or EMA, or one of the procedures administered by competent authorities in the EU member states (decentralized procedure, national procedure or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the European Union. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the European Union, applicants have to demonstrate compliance with all measures included in an EMA-approved Paediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver or (3) a deferral for one or more of the measures included in the PIP.

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The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all EU member states and three of the four European Free Trade Association, or EFTA, States, Iceland, Liechtenstein and Norway. Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the EMA is responsible for conducting the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment. At the end of this period, the EMA's Committee for Medicinal Products for Human Use ("CHMP") provides a scientific opinion on whether or not a marketing authorization should be granted in relation to a medicinal product. Within 15 calendar days of receipt of a final opinion from the CHMP, the European Commission must prepare a draft decision concerning an application for marketing authorization. This draft decision must take the opinion and any relevant provisions of EU law into account. Before arriving at a final decision on an application for centralized authorization of a medicinal product the European Commission must consult the Standing Committee on Medicinal Products for Human Use. The Standing Committee is composed of representatives of the EU member states and chaired by a non-voting European Commission representative. The European Parliament also has a related "droit de regard". The European Parliament's role is to ensure that the European Commission has not exceeded its powers in deciding to grant or refuse to grant a marketing authorization.

Unlike the centralized authorization procedure, the decentralized marketing authorization procedure requires a separate application to, and leads to separate approval by, the competent authorities of each EU member state in which the product is to be marketed. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned EU member states who, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned EU member state cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the European Commission, whose decision is binding on all EU member states.

The mutual recognition procedure similarly is based on the acceptance by the competent authorities of the EU member states of the marketing authorization of a medicinal product by the competent authorities of other EU member states. The holder of a national marketing authorization may submit an application to the competent authority of an EU member state requesting that this authority recognize the marketing authorization delivered by the competent authority of another EU member state.

Regulatory Data Protection in the European Union

In the European Union, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Directive 2001/83/EC. Regulation (EC) No 726/2004 repeats this entitlement for medicinal products authorized in accordance with the centralized authorization procedure. Data exclusivity prevents applicants for authorization of generics of these innovative products from referencing the innovator's data to assess a generic (abbreviated) application for a period of eight years. During an additional two-year period of market exclusivity, a generic marketing authorization application can be submitted and authorized, and the innovator's data may be referenced, but no generic medicinal product can be placed on the European Union market until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of Authorization and Renewals

A marketing authorization has an initial validity for five years in principle. The marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the EU member state. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. The European Commission or the competent authorities of the EU member states may decide, on justified grounds relating to pharmacovigilance, to proceed with one further five year period of marketing authorization. Once subsequently definitively renewed, the marketing authorization shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the European Union market (in case of centralized procedure) or on the market of the authorizing EU member state within three years after authorization ceases to be valid (the so-called sunset clause).

Orphan Drug Designation and Exclusivity

Regulation (EC) No. 141/2000, as implemented by Regulation (EC) No. 847/2000 provides that a drug can be designated as an orphan drug by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the European Union when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that the marketing of the drug in the European Union would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Union or, if such method exists, the drug will be of significant benefit to those affected by that condition.

Once authorized, orphan medicinal products are entitled to 10 years of market exclusivity in all EU member states and in addition a range of other benefits during the development and regulatory review process including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure covering all member countries and a reduction or elimination of registration and marketing authorization fees. However, marketing authorization may be granted to a similar medicinal

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product with the same orphan indication during the 10 year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if this product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, be reduced to six years if it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity

Regulatory Requirements after a Marketing Authorization has been Obtained

In case an authorization for a medicinal product in the European Union is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- Compliance with the European Union's stringent pharmacovigilance or safety reporting rules must be ensured. These rules can impose post-authorization studies and additional monitoring obligations.
- The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable European Union laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with European Union cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the European Union with the intention to import the active pharmaceutical ingredients into the European Union.
- The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the European Union notably under Directive 2001/83/EC, as amended, and EU member state laws.

Regulatory Procedure Governing CE marking Companion Diagnostics in the European Union

In the European Union, *in vitro* medical devices are required to conform with the essential requirements of the European Union Directive on *in vitro* diagnostic medical devices (Directive No 98/79/EC, as amended). To demonstrate compliance with the essential requirements, the manufacturer must undergo a conformity assessment procedure. The conformity assessment varies according to the type of *in vitro* diagnostic medical device. The conformity assessment of *in vitro* diagnostic medical devices can require the intervention of a Notified Body, which is an organization designated by the competent authorities of an EU member state to conduct conformity assessments. The Notified Body will issue a CE Certificate of Conformity following successful completion of a conformity assessment procedure conducted in relation to the *in vitro* diagnostic medical device and its manufacturer and their conformity with the requirements of the Directive. This Certificate entitles the manufacturer to affix the CE mark to its medical device after having prepared and signed a related EC Declaration of Conformity. For *in vitro* diagnostic medical devices which do not require the intervention of a notified body, the manufacturer can issue an EC Declaration of Conformity based on a self-assessment of the conformity of its products with the Essential Requirements laid down in the *in vitro* diagnostic medical device Directive.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. Thereafter, on March 29, 2017, the country formally notified the

European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The withdrawal of the United Kingdom from the European Union will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the United Kingdom provides a notice of withdrawal pursuant to the E.U. Treaty. Since the regulatory framework for pharmaceutical products in the United Kingdom, covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the United Kingdom.

Pharmaceutical Coverage and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use setmelanotide unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Even if setmelanotide is approved, sales will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, such products. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, setmelanotide may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover setmelanotide could reduce physician utilization of our products once approved and have a material adverse effect on our sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor. Third-party reimbursement and coverage may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

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Outside the United States, ensuring adequate coverage and payment for setmelanotide will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of setmelanotide or products to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies or so called Health Technology Assessments, in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other EU member states allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements and interactions with healthcare professionals, third-party payors, and patients, among others, are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, patient privacy laws and regulations and other healthcare laws and regulations that may constrain our business and/or financial arrangements, particularly once third-party reimbursement, including under Medicare, Medicaid or other federally-funded health care programs, becomes available for one or more of our products. The federal and state healthcare laws and regulations that may affect our ability to operate include, but are not limited to the following:

- the United States federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, or receiving remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order or arranging for or recommending the purchase, lease, or order of any good or service, for which payment may be made, in whole or in part, by federal healthcare programs such as Medicare and Medicaid. This statute has been interpreted to apply to arrangements between pharmaceutical companies on one hand and prescribers, purchasers and formulary managers on the other. Liability under the Anti-Kickback Statute may be established without proving actual knowledge of the statute or specific intent to violate it. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. Although there are a number of statutory exemptions and regulatory safe harbors to the federal Anti-Kickback Statute protecting certain common business arrangements and activities from prosecution or regulatory sanctions, the exemptions and safe harbors are drawn narrowly. Practices that involve remuneration to those who prescribe, purchase, or recommend pharmaceutical and biological products, including certain discounts, or engaging such individuals as consultants, advisors and speakers, may be subject to scrutiny if they do not fit squarely within an exemption or safe harbor. Our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability. Moreover, there are no safe harbors for many common practices, such as educational and research grants, charitable donations, product support and patient assistance programs;

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- the federal civil False Claims Act prohibits individuals or entities from, among other things, knowingly presenting, or causing to be presented, a false or fraudulent claim for payment of government funds, or knowingly making, using or causing to made or used a false record or statement material to an obligation to pay money to the government or knowingly concealing or knowingly and improperly avoiding, decreasing, or concealing an obligation to pay money to the federal government. Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Many pharmaceutical manufacturers have been investigated and have reached substantial financial settlements with the federal government under the civil False Claims Act for a variety of alleged improper activities including causing false claims to be submitted as a result of the marketing of their products for unapproved and thus non-reimbursable uses, inflating prices reported to private price publication services which are used to set drug payment rates under government healthcare programs, and other interactions with prescribers and other customers including those that may have affected their billing or coding practices and submission to the federal government. The government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. Pharmaceutical and other healthcare companies also are subject to other federal false claims laws, including, among others, federal criminal healthcare fraud and false statement statutes that extend to non-government health benefit programs;
- the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statement or entry, in connection with the delivery of or payment for healthcare benefits, items or services;
- HIPAA and its implementing regulations, which impose obligations with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal transparency requirements known as the federal Physician Payments Sunshine Act, being implemented as the Open Payments Program requires certain manufacturers of drugs, devices, biologics and medical supplies report payments and other transfers of value to physicians and teaching hospitals, as well as ownership and investments interests held by physicians and their immediate family members. Pharmaceutical and biological manufacturers with products for which payment is available under Medicare, Medicaid or the State Children's Health Insurance Program are required to submit a report to the Centers for Medicare and Medicaid Services within the U.S. Department of Health and Human Services on or before the 90th day of each calendar year disclosing reportable payments made in the previous calendar year; and
- analogous state laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

In addition to the foregoing requirements, several states now require prescription drug companies to report expenses relating to the marketing and promotion of drug products and to report gifts and payments to individual physicians in these states. Other states prohibit various other marketing-related activities. Still other states require the posting of information relating to clinical studies and their outcomes. In addition, California, Connecticut, Nevada, and Massachusetts require pharmaceutical companies to implement compliance programs and/or marketing codes. Several additional states are considering similar proposals. Numerous federal, state and foreign laws and regulations also govern the privacy and security of health

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information and the collection, use, disclosure, and protection of health-related and other personal information, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws, such as Section 5 of the FTC Act, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. Compliance with these laws is difficult and time consuming, and companies that do not comply with these state laws may face civil penalties.

Compliance with such laws and regulations will require substantial resources. If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from government-funded healthcare programs like Medicare and Medicaid, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our financial results.

For additional information regarding obligations under federal health care programs, refer to the risk factor entitled "*If we participate in the Medicaid Drug Rebate Program and fail to comply with our reporting and payment obligations under that program or other governmental pricing programs that we participate in, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.*"

Healthcare Reform

A primary trend in the United States healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the ACA of importance to our potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee does not apply to sales of certain products approved exclusively for orphan indications;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expansion of manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;
- introduction of a price reporting requirement for drugs that are inhaled, instilled, implanted, injected, or infused and not generally dispensed through retail community pharmacies;
- addition of more entity types eligible for participation in the Public Health Service 340B drug pricing program, or the 340B program;

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- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. However, the IPAB implementation has been not been clearly defined. ACA provided that under certain circumstances, IPAB recommendations or recommendations of the Secretary of Health and Human Services will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, beginning April 1, 2013, Medicare payments for all items and services, including drugs and biologics, were reduced by 2% under the sequestration (i.e., automatic spending reductions) required by the Budget Control Act of 2011, as amended by the American Taxpayer Relief Act of 2012. Subsequent legislation extended the 2% reduction, on average, to 2025.

Legislative changes to or regulatory changes under the ACA remain possible and appear likely in the 115th U.S. Congress and under the Trump administration. The nature and extent of any legislative or regulatory changes to the ACA, including repeal and replacement initiatives, are uncertain at this time. It is possible that ACA repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. The scope of potential future legislation to modify or repeal and replace ACA provisions is highly uncertain in many respects.

Employees

We have leveraged skilled experts, consultants, CROs, and contractors to manage our clinical operations, under the leadership and direction of our management. We will expand our infrastructure to manage our clinical, finance and commercial operations with additional full-time employees.

We have 15 employees who are directly employed by us, four of whom hold Ph.D. or M.D. degrees. Of these employees, ten are engaged in development and commercial activities and five are engaged in support administration, including business development and finance. None of these employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationships with these employees to be good.

Facilities

Our offices are located at a 6,830 square foot facility in Boston, Massachusetts used primarily for corporate functions. The lease for this space expires in May 2021.

Legal Proceedings

We are not currently a party to any material legal proceedings.

MANAGEMENT

Executive Officers and Directors

The following table sets forth the names, ages and positions of our directors and executive officers. Each executive officer is employed by us pursuant to a letter agreement entered into as of November 2016 except for Hunter Smith and Nithya Desikan, who entered into letter agreements as of July 2017. Prior to November 2016, each executive officer other than Hunter Smith and Nithya Desikan provided services to us pursuant to the Payroll Services Agreement, which was terminated in November 2016. Each executive officer will be elected annually and will serve until his re-election, or earlier resignation or removal. The executive officers, other than Hunter Smith and Nithya Desikan and directors have served as executive officers and directors of us, the LLC entity, the Predecessor Company and/or the Relamorelin Company during the periods set forth below. We refer to each of these persons as our executive officers.

Name	Age	Position(s)
Keith M. Gottesdiener, M.D.	63	Chief Executive Officer, President and Director
Hunter Smith	49	Chief Financial Officer and Treasurer
Nithya Desikan	38	Chief Commercial Officer
Lex H.T. Van der Ploeg, Ph.D.	63	Chief Scientific Officer
Fred T. Fiedorek, M.D.	62	Chief Medical Officer
Todd Foley(1)	45	Director
Ed Mathers(3)	57	Director
Neil Exter(1)	58	Director
Christophe R. Jean(2)	61	Director
Jonathan T. Silverstein, J.D.(1)(4)	50	Director
David P. Meeker(2)(3)	62	Director and Chairman
David W.J. McGirr(2)(3)	62	Director

(1) Member of Compensation Committee.

(2) Member of Audit Committee.

(3) Member of Governance and Nominating Committee.

(4) Mr. Silverstein will step down from our board of directors effective as of the closing of this offering.

Keith M. Gottesdiener, M.D. | Chief Executive Officer and President

Dr. Gottesdiener has been Chief Executive Officer and a member of the board of directors since October 2011 and was chairman of the board of directors from that date until April 2017. He has been President since August 2017. He joined the Predecessor Company after 16 years at Merck Research Laboratories, or Merck. Dr. Gottesdiener joined Merck early clinical development in 1995, helping to transition compounds from the bench to the bedside and through to proof of concept. He held positions of increasing responsibility, eventually leading Merck's early clinical development across all therapeutic areas from 2001 through early 2006. From 2006 to 2011, he was a leader of Merck's late clinical development organization, first overseeing the development of Merck's infectious diseases and vaccine products through pivotal trials, registration, and life cycle management, including Gardasil™ (HPV Vaccine), Rotateq™ (rotavirus vaccine), Zostavax™ (zoster vaccine) and Isentress™ (HIV integrase inhibitor), among others. In 2008, Dr. Gottesdiener was appointed Late Stage Therapeutic Group Leader, and in that role led Merck's late-stage clinical development efforts (from Phase 2 thru patent expiry) across all therapeutic areas. After Merck's merger with Schering Plough in 2009, he continued as co-head of late development. Dr. Gottesdiener received his B.A. from Harvard College and his M.D. from the University of Pennsylvania. He completed his residency and fellowship at the Brigham and Women's Hospital-Beth Israel Medical Center-Dana Farber Cancer Institute Children's Hospital programs. After his fellowship,

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Dr. Gottesdiener did postdoctoral research in the laboratory of Dr. Jack Strominger at Dana Farber Cancer Institute working on the molecular immunology of the T-cell receptor. In 1986, he joined the faculty as an assistant professor at Columbia University, started an independent research laboratory with NIH RO-1 funding, focusing on gene transcription, and was Associate Clinical Professor of Medicine at the time he left to join Merck in 1995. Dr. Gottesdiener was a director and the chief executive officer of the Relamorelin Company until December 2016. Dr. Gottesdiener is currently a director of Intercept Pharmaceuticals and the LLC entity. In addition, Dr. Gottesdiener is the chief executive officer of the LLC entity, a position from which he will resign prior to the consummation of this offering. We believe that Dr. Gottesdiener's detailed knowledge of our company, his extensive experience in the pharmaceutical industry as a senior executive, and his research work for both medical and academic institutions provide him with the qualifications to serve as director of our company.

Hunter Smith | Chief Financial Officer and Treasurer

Mr. Smith has been Chief Financial Officer since July 2017 and Treasurer since August 2017. He has more than 20 years of global finance and management experience across multiple industries and financial disciplines, including expertise in business analysis and planning, mergers and acquisitions, capital raising and investor relations. Previously, he was Vice President, Finance and Chief Financial Officer of the Inflammation and Immunology Business Unit at Celgene Corporation from 2013 to July 2017. In this role, Mr. Smith provided finance leadership for the global launch of Otezla®, co-led the integration of Receptos, Inc. following its acquisition by Celgene, and led global business planning and analysis for commercial affiliates and clinical study activities in over 16 countries. Before joining Celgene, Mr. Smith worked in roles of increasing responsibility at Bunge Limited from 1999 to 2013, including Director of Investor Relations, Chief Financial Officer—Asia, Corporate Treasurer, and Chief Financial Officer of Bunge's Sugar and Bioenergy Segment. Mr. Smith also serves as an Independent Director of Genessee & Wyoming Inc. and is a member of its compensation committee. Mr. Smith holds an MBA in Finance from New York University's Stern School of Business and a B.A. in History, with honors, from Northwestern University.

Nithya Desikan | Chief Commercial Officer

Ms. Desikan has been Chief Commercial Officer since July 2017. She has over 15 years of experience commercializing new therapies in domestic and global markets. Previously, Ms. Desikan worked at Biogen Inc., where she served most recently as Vice President and Asset Executive, from September 2016 to July 2017, overseeing global profit and loss account for TEZELA® and supporting the product's position as the #1 prescribed oral therapy in multiple sclerosis and from November 2015 to September 2016, building a team to support the Biogen pipeline for the clinical development of inflammatory bowel disease. Prior to that, Ms. Desikan held the role of Vice President and Program Executive from September 2014 to November 2015, where she led Biogen's Hematology business, now the Biogen spin-off, Bioverativ, to drive the growth of ALPROLIX® and ELOCTATE® and the development of multiple preclinical assets. Before that, from February 2012 to September 2014, Ms. Desikan built the strategy to support the U.S. launch of ALPROLIX, Biogen's first entrant into the orphan hemophilia market. Before joining Biogen Inc., Ms. Desikan spent 12 years at Johnson & Johnson in the United States and China, supporting brands including: XARELTO®, LEVAQUIN®, TOPAMAX®, ULTRACET®, NUCYNTA®, NUCYNTA®ER and VELCADE®. Ms. Desikan holds a B.S. in Material Science Engineering, with honors, from the University of Florida.

Lex H.T. Van der Ploeg, Ph.D. | Chief Scientific Officer

Dr. Van der Ploeg has been Chief Scientific Officer since October 2011. He has more than 25 years of drug development experience focused on obesity, metabolic disorders, oncology, and neurodegenerative diseases. Before joining the Predecessor Company, he was Senior Vice President of Integrative Medicine

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and Translational Science at Abraxis Bioscience and Head of R&D at Abraxis Health; both companies were acquired by Celgene Corporation. Prior to that, he held R&D leadership roles at Merck directing drug development programs in metabolism, oncology, and neurodegenerative diseases as Vice President, Basic Research and Site Head, Merck Boston; Site Head, Merck San Diego; and Head, Obesity Research for Merck Rahway and Banyu, Japan. Previously, Dr. Van der Ploeg was an associate professor in the Department of Genetics and Development at Columbia University. He has received numerous awards and grants for his research and has published more than 200 peer-reviewed research papers. Dr. Van der Ploeg is a named inventor on more than 50 patents and patent applications. Dr. Van der Ploeg was the Chief Scientific Officer of the Relamorelin Company was until December 2016. Dr. Van der Ploeg is currently the Chief Scientific Officer of the LLC entity, a position from which he will resign prior to the consummation of this offering. He received an M.S. in Biochemistry from the University of Amsterdam and a Ph.D. in Biochemistry/Enzymology/Genetics from the University of Amsterdam/Netherlands Cancer Institute.

Fred T. Fidorek, M.D. | Chief Medical Officer

Dr. Fidorek has been Chief Medical Officer since October 2014, joining us after nearly 14 years at Bristol-Myers Squibb, or BMS. He has extensive drug development experience across many therapeutic areas, ranging from early development through Phase 4 and commercial launch. Dr. Fidorek has particular expertise in diabetes, metabolic disorders and cardiovascular disease, most recently serving as Senior Vice President, Head of Cardiovascular and Metabolic Development at BMS, where he led Phase 2 through Phase 4 global development for these therapeutic areas. Under his leadership, several new medicines achieved successful marketing authorization, including Onglyza® (saxagliptin), Farxiga™ (dapagliflozin), Eliquis® (apixaban), Myalept™ (metreleptin), Bydureon® Dual Chamber Pen, and Glucovance® (metformin/glyburide). While at BMS, Dr. Fidorek also co-led exploratory development, helping to transition compounds from discovery stage to proof of concept patient trials. In addition, Dr. Fidorek co-directed the Clinical Science Committee charged with providing scientific, regulatory, and biostatistical review of Phase 1 through Phase 4 clinical trials; he was a member of the Medical Review Group charged with oversight of potential emerging safety signals from marketed medicines or compounds in development; and he participated in joint development committees for BMS alliances with Astra-Zeneca, Pfizer, Otsuka, KAI Pharmaceuticals, Solvay, and Merck. Prior to joining BMS, Dr. Fidorek held positions of increasing responsibility at Glaxo-Wellcome in Research Triangle Park, or RTP, and was International Project Leader for a Phase 3 metabolic drug development program prior to his move to BMS. Dr. Fidorek was the Chief Medical Officer of the Relamorelin Company until December 2016. Dr. Fidorek is currently the Chief Medical Officer of the LLC entity, a position from which he will resign prior to consummation of this offering. Dr. Fidorek received his B.A. from Yale University and his M.D. from Harvard Medical School. He completed residency and fellowship training in Internal Medicine and Endocrinology & Metabolism at Washington University in St. Louis, including post-doctoral research on the genetics of animal models of diabetes and obesity. He also served on the faculties at Washington University School of Medicine in St. Louis and the University of North Carolina in Chapel Hill School of Medicine, including an adjunct clinical appointment while at Glaxo-Wellcome in RTP.

Todd Foley

Mr. Foley has served as a member of our board of directors since July 2014. Mr. Foley is a managing director with MPM Capital, a venture capital firm, which he joined in 1999. Prior to joining MPM, Mr. Foley worked in business development at Genentech and in management consulting with Arthur D. Little. Mr. Foley currently serves as a member of the board of directors of Chiasma, Inc., Clinical Ink, Inc., Iconic Therapeutics, Inc., Repare Therapeutics Inc., Semma Therapeutics, Inc., Switch Bio, Inc. and Tetherex Pharmaceuticals, Inc. Mr. Foley received a B.S. in chemistry from the Massachusetts Institute of Technology and an MBA from Harvard Business School. We believe that Mr. Foley's broad experience in

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the life sciences industry as a venture capitalist, as well as his service on the boards of directors of numerous companies provide him with the qualifications to serve as a director of our company.

Ed Mathers

Mr. Mathers has served as a member of our board of directors since March 2013. He has been a Partner at New Enterprise Associates, or NEA, a venture capital firm, since August 2008. Mr. Mathers currently serves on the boards of directors of Amplyx Pharmaceuticals, Inc., Envisia Therapeutics Inc., Intarcia Therapeutics, Inc., Inozyme Pharma, Inc., Liquidia Technologies, Inc., Lumos Pharma, Inc., Lumena Pharmaceuticals, Inc., Mirna Therapeutics, Inc., ObsEva SA, Ra Pharmaceuticals, Inc., Satori Pharmaceuticals Incorporated, Senti Biosciences and Synlogic, LLC, all of which are biotechnology companies. In addition, Mr. Mathers is a member of the Biotechnology Industry Organization board, the Southeast BIO board and the North Carolina State Physical and Mathematical Sciences Foundation board. Prior to joining NEA, Mr. Mathers served in various corporate development roles at MedImmune, Inc., a biotechnology company that was acquired by AstraZeneca PLC in 2007, culminating in the position of Executive Vice President, Corporate Development and Venture. In this role, he also led the company's venture capital subsidiary, MedImmune Ventures, Inc., from 2002 to 2008. Mr. Mathers was a director of MedImmune, LLC, from 2007 to 2008. From 2000 to 2002, Mr. Mathers was Vice President, Marketing and Corporate Licensing and Acquisitions at Inhale Therapeutic Systems, Inc., a biopharmaceutical company, which is now known as Nektar Therapeutics, Inc. Previously, for 15 years, Mr. Mathers was at Glaxo Wellcome, Inc., where he held sales and marketing positions of increasing responsibility. Mr. Mathers received a B.S. in chemistry from North Carolina State University. We believe that Mr. Mathers' extensive experience in the life sciences industry as a venture capitalist and senior executive, as well as his service on the boards of directors of numerous companies provide him with the qualifications to serve as a director of our company.

Neil Exter

Mr. Exter has served as a member of our board of directors since April 2014. He is a partner at Third Rock Ventures, where he plays an integral role in the formation, development, business strategy, and business development efforts of portfolio companies. He has more than 20 years of business development and strategic experience, facilitating the successful development and implementation of operations and collaborations across the spectrum of newly emerging and established biotech companies. Mr. Exter is currently the interim chief operating officer of Goldfinch Bio. Prior to joining Third Rock Ventures, Mr. Exter was CBO of Alantos Pharmaceuticals and led the sale of that company to Amgen. Previously, he served as Vice President of Business Development for Millennium Pharmaceuticals. Mr. Exter is a board member of CytomX Therapeutics, Cibiem, Lotus Tissue Repair, Coridea NC1, Coridea NC2, Element Science, Goldfinch Bio, Pliant Therapeutics, Revolution Medicine, and Seventh Sense. He is a member of the Research Committee of Children's Hospital Boston, the investment committee of the Innovation Research Fund at Partners Healthcare, the Board of Directors of the New England Venture Capital Association, the Advisory Council of the Electrical and Computer Engineering Department at Cornell University, and the Board of Visitors of Columbia College. He holds an MBA as a Baker Scholar from Harvard Business School, an M.S. from Stanford University, and a B.S. from Cornell University. We believe that Mr. Exter's extensive experience in the life sciences industry as a venture capitalist and senior executive, as well as his service on the boards of directors of numerous companies provide him with the qualifications to serve as a director of our company.

Christophe R. Jean

Mr. Jean has served as a member of our board of directors since April 2015. He is Executive Vice President of Corporate Strategy, Business Development, Alliances and M&A for the Ipsen Group, a position he assumed in 2013 after serving for 11 years in the position of Executive Vice-President, Chief

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Operating Officer, with responsibility for all commercial operations and medical affairs worldwide as well as Ipsen's therapeutic area franchises. Prior to joining Ipsen, Mr. Jean was President and CEO for the pharmaceutical activities of the Pierre Fabre Group and President of Europe, Middle East, and Africa for Novartis' Pharmaceutical Division. Prior to the merger of Ciba-Geigy and Sandoz that formed Novartis, he held a number of marketing and management positions in Europe and Latin America for Ciba-Geigy, culminating as Head of Finance and IT Worldwide and Member of the Pharma Executive Committee. Mr. Jean is a member of the Ipsen Group Executive Committee, the Supervisory Board of Diaxonhit, and the European Biopharmaceutical Enterprises Board. He holds an MBA from Harvard Business School. We believe that Mr. Jean's extensive experience in the life sciences industry as a senior executive provides him with the qualifications to serve as a director of our company.

Jonathan T. Silverstein, J.D.

Mr. Silverstein has served as a member of our board of directors since August 2015. He is a Partner and a Co-Head of Global Private Equity at OrbiMed, the world's largest fully dedicated healthcare fund manager. Mr. Silverstein joined OrbiMed in 1999 to focus on private equity and structured transactions in small-capitalization public biotechnology and medical device companies. From 2012 through 2016, *Forbes®* magazine has named Mr. Silverstein one of the top 100 venture capitalists in the world in its "Forbes Midas List" of top technology investors. Mr. Silverstein has a J.D. and an M.B.A. from the University of San Diego, and a B.A. in Economics from Denison University. We believe that Mr. Silverstein's extensive experience in life sciences venture capital provides him with the qualifications to serve as a director for our company. Mr. Silverstein will step down from our board of directors effective as of the closing of this offering.

David P. Meeker

Dr. Meeker has served as a member of our board of directors since November 2015 and became chairman of the board in April 2017. Dr. Meeker has served as President and Chief Executive officer of Genzyme, a unit of Sanofi, a global biotechnology company, since October 2011. Dr. Meeker oversees the company's two business units—Rare Diseases and Multiple Sclerosis. As an Executive Vice President of Sanofi, he is a member of Sanofi's Executive Committee. Dr. Meeker joined Genzyme in 1994 as Medical Director to work on the Cystic Fibrosis Gene Therapy program. Subsequently, as Vice President, Medical Affairs, he was responsible for the development of rare disease therapies that today represent transformative and life-saving advancements in medicine for patients. Prior to Genzyme's merger with Sanofi in 2011, Dr. Meeker was Genzyme's Chief Operating Officer, responsible for its commercial organization, overseeing its business units, country management organization and global market access functions. He played an important role in the integration with Sanofi. Prior to joining Genzyme, Dr. Meeker was the director of the Pulmonary Critical Care Fellowship at the Cleveland Clinic and an assistant professor of medicine at Ohio State University. Dr. Meeker is currently a member of the board of directors of MyoKardia, Inc. He has authored more than 40 articles and multiple book chapters. Dr. Meeker received his M.D. from the University of Vermont Medical School. He completed the Advanced Management Program at Harvard Business School in 2000. We believe that Dr. Meeker's deep experience as a senior executive at global pharmaceutical companies and involvement in the development and commercialization of pharmaceutical product candidates for the treatment of rare and ultra-rare diseases provide him with the qualifications to serve as a director of our company.

David W.J. McGirr

Mr. McGirr has served as a member of our board of directors since November 2015. Mr. McGirr serves as a director of Relypsa, Inc., a pharmaceutical company focused on polymer science, Insamed Incorporated, a pharmaceutical company devoted to the treatment of rare diseases, and Roka Bioscience, a molecular diagnostics company. From March 2013 until June 2014, Mr. McGirr was Senior Advisor to

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the chief executive officer of Cubist Pharmaceuticals and from November 2002 to March 2013, Mr. McGirr was Senior Vice President and Chief Financial Officer of Cubist. Prior to joining Cubist in 2002, Mr. McGirr was the President and Chief Operating Officer of hippo inc, an internet technology, venture-financed company. Mr. McGirr served as a member of hippo's board of directors from 1999 to 2003. From 1996 to 1999, he was the President of GAB Robins North America, Inc., a risk management company, serving also as Chief Executive Officer from 1997 to 1999. Mr. McGirr was a private equity investor from 1995 to 1996. From 1978 to 1995, Mr. McGirr served in various positions within the S.G. Warburg Group, ultimately as Chief Financial Officer, Chief Administrative Officer and Managing Director of S.G. Warburg & Co., Inc., a position held from 1992 to 1995. Mr. McGirr received a B.Sc. in Civil Engineering from the University of Glasgow and received an M.B.A. from The Wharton School at the University of Pennsylvania. Mr. McGirr has been designated an audit committee financial expert as defined in applicable SEC rules. We believe that Mr. McGirr's senior-level executive experience in a variety of industries, including in the life sciences industry, provides him with the qualifications to serve as a director of our company.

Composition of the Board of Directors after this Offering

Our amended and restated bylaws will provide that our board of directors will consist of such number of directors as our board of directors may determine from time to time. Our board of directors currently consists of eight directors. Immediately upon the consummation of this offering, our board of directors will consist of (i) one director designated by MPM Capital, who is currently Todd Foley, and who will be continuing as a director following the offering, (ii) one director designated by NEA, who is currently Ed Mathers, and who will be continuing as a director following the offering, (iii) one director designated by Third Rock Ventures, who is currently Neil Exter, and who will be continuing as a director following the offering, (iv) one director designated by Sutrepa SAS, who is currently Christophe Jean, and who will be continuing as a director following the offering, and (v) David Meeker, David McGirr and our chief executive officer, each of whom will be continuing as a director following the offering. Our board of directors has determined that all of our directors, other than Dr. Gottesdiener, our chief executive officer, are independent for the purpose of serving on our board of directors under the independence standards promulgated by NASDAQ.

Our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing of this offering will provide that our board of directors will be divided into three classes, Class I, Class II and Class III, with members of each class serving staggered three-year terms. Upon the closing of this offering, the members of the classes will be divided as follows

- our Class I directors will be Keith Gottesdiener and Christophe Jean, and their terms will expire at the annual meeting of stockholders to be held in 2018;
- our Class II directors will be Ed Mathers, Todd Foley and Neil Exter, and their terms will expire at the annual meeting of stockholders to be held in 2019; and
- our Class III directors will be David Meeker and David McGirr, and their terms will expire at the annual meeting of stockholders to be held in 2020.

Upon the expiration of the term of a class of directors, directors in that class will be eligible to be elected for a new three-year term at the annual meeting of stockholders in the year in which their term expires.

Board Leadership Structure

The positions of chairman of the board and chief executive officer are presently separated. Our board of directors recognizes the time, effort and energy that the chief executive officer is required to devote to his position in the current business environment, as well as the commitment required to serve as our

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chairman, particularly as the board of directors' oversight responsibilities continue to grow. Our board of directors believes that having separate positions is the appropriate leadership structure for us at this time and demonstrates our commitment to good corporate governance.

Board Committees

Our board of directors has established the following committees: an audit committee, a compensation committee and a governance and nominating committee. The initial composition and responsibilities of each committee are described below. Members will serve on these committees until their resignation or until otherwise determined by our board of directors.

Audit Committee

Our audit committee will provide oversight of our accounting and financial reporting process, the audit of our financial statements and our internal control function. Among other matters, the audit committee will be responsible for the following: assisting the board of directors in oversight of the independent auditors' qualifications, independence and performance; the engagement, retention and compensation of the independent auditors; reviewing the scope of the annual audit; reviewing and discussing with management and the independent auditors the results of the annual audit and the review of our quarterly financial statements, including the disclosures in our annual and quarterly reports filed with the SEC; reviewing our risk assessment and risk management processes; establishing procedures for receiving, retaining and investigating complaints received by us regarding accounting, internal accounting controls or audit matters; and approving audit and permissible non-audit services provided by our independent auditor.

The current members of our audit committee are David McGirr, who is the chair of the committee, Christophe Jean, and David Meeker. All members of our audit committee meet the requirements for financial literacy under the applicable rules and regulations of the SEC and NASDAQ. Our board of directors has determined that David McGirr is an audit committee financial expert as defined under the applicable rules of the SEC and has the requisite financial sophistication as defined under the applicable rules and regulations of NASDAQ. All of the members of our audit committee are independent directors as defined under the applicable rules and regulations of the SEC and NASDAQ.

Compensation Committee

Our compensation committee will adopt and administer the compensation policies, plans and benefit programs for our executive officers and all other members of our executive team. Our compensation committee will also be responsible for making recommendations regarding non-employee director compensation to the full board of directors. In addition, among other things, our compensation committee will evaluate annually, in consultation with the board of directors, the performance of our chief executive officer, review and approve corporate goals and objectives relevant to compensation of our chief executive officer and other executives and evaluate the performance of these executives in light of those goals and objectives. Our compensation committee will also adopt and administer our equity compensation plans. The current members of our compensation committee are Neil Exter, who is the chair of the committee, Todd Foley, and Jonathan Silverstein. Following consummation of this offering Messrs. Exter and Foley will comprise our compensation committee. All of the members of our compensation committee are independent under the applicable rules and regulations of the SEC and NASDAQ, and qualify as outside directors under Section 162(m) of the Code.

Governance and Nominating Committee

Our governance and nominating committee will be responsible for, among other things, making recommendations regarding corporate governance, the composition of our board of directors, the

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identification, evaluation and nomination of director candidates and the structure and composition of committees of our board of directors. In addition, our governance and nominating committee will oversee our corporate governance guidelines, approve our committee charters, oversee compliance with our code of business conduct and ethics, contribute to succession planning, review policies and procedures with respect to our related party transactions policy and oversee the board self-evaluation process. The current members of our governance and nominating committee are David Meeker, who is the chair of the committee, Ed Mathers, and David McGirr. All of the members of our governance and nominating committee are independent under the applicable rules and regulations of NASDAQ.

Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee is or has at any time during the past year been one of our officers or employees. None of our executive officers currently serves or in the past year has served as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving on our board of directors or compensation committee.

Board Observer Rights

In connection with this offering, the board of directors invited Sara Brownstein of Baker Bros. Advisors LP to continue to attend all meetings of the board of directors in a nonvoting observer capacity. The board of directors may terminate the board observer rights in its sole discretion. See "Certain Relationships and Related Party Transactions—Transactions with Baker Bros. Advisors LP."

Role of the Board in Risk Oversight

The audit committee of the board of directors is primarily responsible for overseeing our risk management processes on behalf of the board of directors. Going forward, we expect that the audit committee will receive reports from management at least quarterly regarding our assessment of risks. In addition, the audit committee reports regularly to the board of directors, which also considers our risk profile. The audit committee and the board of directors focus on the most significant risks we face and our general risk management strategies. While the board of directors oversees our risk management, management is responsible for day-to-day risk management processes. Our board of directors expects management to consider risk and risk management in each business decision, to proactively develop and monitor risk management strategies and processes for day-to-day activities and to effectively implement risk management strategies adopted by the audit committee and the board of directors. We believe this division of responsibilities is the most effective approach for addressing the risks we face and that the leadership structure of our board of directors, which also emphasizes the independence of the board of directors in its oversight of its business and affairs, supports this approach.

Scientific Advisory Board

Our management team is supported by a scientific advisory board composed of leading academic and industry scientists. This group generally meets quarterly with our management team either as a group or

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individually to provide advice and guidance on our development programs. Our scientific advisory board consists of:

John Amatruda, M.D.	Dr. Amatruda has broad clinical development expertise in metabolic disease. Most recently, he was Senior Vice President and Franchise Head for Diabetes and Obesity at Merck & Co., Inc.
Michael Camilleri, M.D.	Dr. Camilleri is a Professor of Medicine and Physiology in the Mayo Clinic College of Medicine. He is a leading expert in gastroenterology, with a research focus on enteric neurosciences and the physiology, pathophysiology, and treatment of diseases that affect gastrointestinal motility, including gastroparesis, diabetes, obesity, and irritable bowel syndrome.
William Chin, M.D.	Dr. Chin is Chief Medical Officer and Executive Vice President at PhRMA. Formerly, he was Executive Dean for Research at Harvard Medical School, following a 10-year career at Eli Lilly and Company, where he was most recently Senior Vice President for Discovery Research and Clinical Investigation.
Lee Kaplan, M.D., Ph.D. <i>Chairman</i>	Dr. Kaplan is Director of the Obesity, Metabolism, & Nutrition Institute and was Founding Director of the Weight Center at the Massachusetts General Hospital. He is an Associate Professor of Medicine at Harvard Medical School.
Elizabeth Stoner, M.D.	Dr. Stoner is a founder of the LLC entity and served as our Chief Development Officer from 2010 through 2014. Dr. Stoner previously served in various roles at Merck, most recently as Senior Vice President of Global Clinical Development Operations, and is a Managing Director at MPM Ventures.

Code of Business Conduct and Ethics

We have adopted a code of business conduct and ethics that will apply to all of our employees, including our executive officers, and directors, and those employees responsible for financial reporting. The code of business conduct and ethics will be available on our website. We expect that, to the extent required by law, any amendments to the code, or any waivers of its requirements, will be disclosed on our website.

EXECUTIVE AND DIRECTOR COMPENSATION

This section discusses the material elements of compensation for our named executive officers and the most important factors relevant to an analysis of these policies. It provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our executive officers named in the "Summary Compensation Table" below, or our named executive officers, and is intended to place in perspective the data presented in the following tables and the corresponding narrative. Our named executive officers are Keith M. Gottesdiener, M.D., Bart Henderson, our former president, and Fred T. Fidorek, M.D. Each of our named executive officers is or was an employee of us pursuant to a letter agreement entered into November 2016, or the letter agreements. Prior to entering into the letter agreements, each of our named executive officers was an employee of the Relamorelin Company and provided services to us pursuant to a Payroll Services Agreement with the Relamorelin Company. The compensation discussed below was paid to our executive officers by us and/or the Relamorelin Company and the compensation decisions discussed below were made either by the compensation committee of the LLC entity's board of managers, which we refer to as the LLC committee, or the compensation committee of our board of directors, which we refer to as the committee.

In preparing to become a public company, we have begun a thorough review of all elements of the compensation of our executives, including our compensation philosophy and the function and design of our equity incentive programs. We have begun and expect to continue to evaluate the existing executive compensation program to ensure our program is competitive with the companies with which we compete for executive talent and is appropriate for a public company.

Summary Compensation Table

The following table presents compensation awarded in 2016 and 2015, to our named executive officers or accrued for those executive officers for services rendered during 2016 and 2015.

<u>Name & Principal Position</u>	<u>Year</u>	<u>Salary (\$)</u>	<u>Stock Awards (\$)⁽¹⁾</u>	<u>Option Awards (\$)⁽²⁾</u>	<u>Non-Equity Incentive Plan Compensation (\$)⁽³⁾</u>	<u>Total (\$)⁽⁴⁾</u>
Keith M. Gottesdiener, M.D. <i>Chief Executive Officer and President</i>	2016	\$ 476,500	—	—	\$ 85,770	\$ 562,270
	2015	\$ 463,508	—	\$ 1,282,757	\$ 231,754	\$ 1,978,019
Bart Henderson <i>Former President</i>	2016	\$ 339,000	—	—	\$ 54,240	\$ 393,240
	2015	\$ 329,772	—	\$ 579,871	\$ 131,909	\$ 1,041,552
Fred T. Fidorek, M.D. <i>Chief Medical Officer</i>	2016	\$ 344,400	—	—	\$ 37,195	\$ 381,595
	2015	\$ 335,000	\$ 567,934	\$ 349,164	\$ 117,250	\$ 1,369,348

- (1) Reflects the full grant date fair value of restricted common units of the LLC entity granted by the LLC entity in 2015.
- (2) The amounts reflect the full grant date fair value for awards granted during 2015. The grant date fair value was computed in accordance with ASC Topic 718, Compensation—Stock Compensation. The assumptions we used in valuing options are described in Note 7 to our audited financial statements contained herein.
- (3) Amounts represent incentive payments earned in 2016 and paid during 2017, or earned in 2015 and paid during 2016, as applicable, based on achievement of performance goals and other factors.
- (4) Reflects compensation for services by the named executive officers. Pursuant to the Payroll Services Agreement, the 2015 and part of the 2016 costs were shared with the Relamorelin Company on a proportional use basis. Costs have been allocated consistent with Staff Accounting Bulletin Topic 1B.

Executive Compensation

Overview

Our executive compensation program is based on a pay-for-performance philosophy. The committee designed our executive compensation program to achieve the following primary objectives: provide compensation and benefit levels that will attract, retain, motivate and reward a highly talented executive team within the context of responsible cost management; establish a direct link between our individual/team performance and results and our executives' compensation; and align the interests and objectives of our executives with those of our stockholders by linking executive equity awards to stockholder value creation. The compensation program for our executive officers is composed primarily of the following three main components: base salary, annual cash incentives and long-term equity incentives.

Base Salary

The 2016 base salaries were determined for each named executive officer by the committee, which gives consideration to each officer's experience, expertise and performance, as well as market compensation levels for similar positions.

Name	2016 Base Salary (\$)
Keith M. Gottesdiener, M.D.	476,500
Bart Henderson	339,000
Fred T. Fidorek, M.D.	344,400

The 2016 base salary for each named executive officer became effective on January 1, 2016.

Annual Performance-Based Incentive Opportunity

In addition to base salaries, our named executive officers are eligible to receive annual performance-based cash incentives, which are designed to motivate our executives to achieve defined annual corporate goals and to reward our executives for their contributions towards achievement of these goals. The annual performance-based incentive each named executive officer was eligible to receive in 2016 was generally based on the extent to which the officer achieved the corporate goals that the LLC committee established at the beginning of 2016. After the end of 2016, the committee reviewed performance against each goal and determined the extent to which each goal was achieved.

The committee generally considered each named executive officer's individual contributions towards reaching the annual corporate goals but did not establish specific individual goals for each of them. Pursuant to the terms of their respective agreements governing their employment relationship, described below under "Agreements with our Named Executive Officers," Dr. Gottesdiener is eligible to receive a target bonus of up to 50% of his base salary, Mr. Henderson while serving as an executive officer, was eligible to receive a target bonus of up to 50% of his base salary, and Dr. Fidorek is eligible to receive a target bonus of up to 35% of his base salary. However, there is no minimum bonus percentage or amount established for the named executive officers and, as a result, the bonus amounts have varied from year to year based on corporate and individual performance.

In December 2016, the committee reviewed the 2016 corporate goals and determined that on an overall basis, significant progress had been made towards achieving all of those goals. In recognition of this achievement and the efforts of each executive, the committee awarded each of our named executive officers eligible for performance bonuses a portion of their target bonus opportunity for 2016. For 2016, Dr. Gottesdiener received an aggregate bonus of \$246,589, \$160,819 of which was paid by the Relamorelin Company and \$85,770 of which was paid by us. Mr. Henderson received an aggregate bonus of \$155,940, \$101,700 of which was paid by the Relamorelin Company and \$54,240 of which was paid by us, and

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Dr. Fidorek received an aggregate bonus of \$114,685, \$77,490 of which was paid by the Relamorelin Company and \$37,195 of which was paid by us.

Outstanding Equity Awards at End of 2016

The following table provides information about outstanding equity awards held by each of our named executive officers at December 31, 2016. All options were granted under the 2015 Plan.

Name	Option Awards ⁽¹⁾⁽²⁾				Stock Awards	
	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price (\$)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested	Market Value of Shares or Units or Other Rights That Have Not Vested
Keith M. Gottesdiener, M.D.	91,602(3)	167,038	\$ 4.59	11/16/2025	—	—
	20,276(3)	36,975	\$ 7.52	12/30/2025	—	—
	—	—	—	—	23,000(5)	\$ 421,130
Bart Henderson	42,185(3)	76,926	\$ 4.59	11/16/2025	—	—
	8,690(3)	15,846	\$ 7.52	12/30/2025	—	—
	—	—	—	—	12,000(5)	\$ 219,720
Fred T. Fidorek, M.D.	28,268(3)	51,547	\$ 4.59	11/16/2025	—	—
	3,476(4)	6,338	\$ 7.52	12/30/2025	—	—
	—	—	—	—	51,443(6)	\$ 941,921

- (1) These options vest in 48 equal monthly installments, starting on August 3, 2015, except that the last installment, if necessary, may be smaller.
- (2) Upon an option holder's termination of employment on account of the option holder's death or disability, these options expire on the first anniversary of the option holder's termination. If an option holder's employment terminates for any other reason, these options expire three months after the option holder's termination.
- (3) If the option holder's employment is terminated within the three months preceding or the 12 months immediately following a change of control of us, 100% of the option holder's equity awards will become immediately exercisable.
- (4) If the option holder's employment is terminated within the three months preceding or the 12 months immediately following a sale of us (as defined in his previous letter agreement with the Relamorelin Company and his current letter agreement with us), the vesting of all of the option holder's equity awards, including these options, will be accelerated such that up to 50% of the option holder's equity awards will become immediately exercisable. If, at the time of the change of control, 50% of the option holder's equity awards are already vested, there will be no further acceleration of vesting.
- (5) Represents the unvested portion of restricted common units of the LLC entity granted by the LLC entity on March 21, 2013. The restricted common units vested fully upon the Distribution.
- (6) Represents the unvested portion of restricted common units of the LLC entity granted by the LLC entity on June 1, 2015. The restricted common units vest in 48 equal monthly installments beginning October 21, 2014.
- (7) Mr. Henderson resigned from employment with us in June 2017, but pursuant to the terms of his consulting agreement with us, he will continue to vest in any restricted equity held by him through and including December 31, 2017.

Pension Benefits

Our named executive officers did not participate in, or otherwise receive any benefits under, any pension or retirement plan during 2016, other than pursuant to the 401(k) plan described under "401(k) Plan."

Nonqualified Deferred Compensation

Our named executive officers did not participate in, or earn any benefits under, a nonqualified deferred compensation plan during 2016.

Agreements with our Named Executive Officers

In November 2016, each named executive officer entered into a letter agreement with us on the terms as described below. On September 13, 2017, upon the recommendation of our committee as we prepare to become a public company, our named executive officers except for Bart Henderson who entered into a consulting agreement with us on June 12, 2017, entered into new letter agreements with us on terms substantially similar to those described below except as described below under "—Terms and Conditions of New Agreements with our Named Executive Officers."

Agreement with Dr. Gottesdiener. Under Dr. Gottesdiener's letter agreement, he is entitled to an annual base salary of \$476,500, subject to adjustment in the committee's sole discretion, is eligible to receive an annual target performance bonus of up to 50% of his base salary, as determined by the committee, and is entitled to certain severance benefits, the terms of which are described below under "—Potential Payments Upon Termination or Change of Control."

Agreement with Mr. Henderson. Under Mr. Henderson's letter agreement, he is entitled to an annual base salary of \$335,000, subject to adjustment in the committee's sole discretion, is eligible to receive an annual target performance bonus of up to 50% of his base salary, as determined by the committee, and is entitled to certain severance benefits, the terms of which are described below under "—Potential Payments Upon Termination or Change of Control."

On June 12, 2017, Mr. Henderson resigned his employment and entered into a consulting agreement with us to provide transition services.

Agreement with Dr. Fiedorek. Under Dr. Fiedorek's letter agreement, he is entitled to an annual base salary of \$344,400, subject to adjustment in the committee's sole discretion, is eligible to receive an annual target performance bonus of up to 35% of his base salary, as determined by the committee, and is entitled to certain severance benefits, the terms of which are described below under "—Potential Payments Upon Termination or Change of Control."

Potential Payments Upon Termination or Change of Control

Regardless of the manner in which a named executive officer's employment terminates, each named executive officer is entitled to receive amounts earned during his term of employment, including salary and unused vacation pay. In addition, each of our named executive officers is eligible to receive certain benefits pursuant to his letter agreement as described below.

Dr. Gottesdiener. Under the terms of Dr. Gottesdiener's letter agreement, upon termination without "cause," as defined below, or for "good reason," as defined below, subject to customary conditions, including his execution and nonrevocation of an acceptable release, Dr. Gottesdiener will be entitled to receive a severance payment in an aggregate amount equal to 12 months of his base salary then in effect, paid in substantially equal installments over a period of 12 months in accordance with ordinary payroll practices.

Upon a termination without "cause" or for "good reason" within the three months immediately preceding or the 12 months immediately following a "sale of the company" as defined in the letter agreement, subject to customary conditions, including his execution and nonrevocation of an acceptable release, Dr. Gottesdiener, in lieu of the above benefits, will be entitled to receive a severance payment in an aggregate amount equal to 12 months of his base salary then in effect, paid in substantially equal installments over a period of 12 months in accordance with ordinary payroll practices, and a payment equal to 100% of his annual target bonus for the year in which the termination occurs. In addition, each unvested equity award held by Dr. Gottesdiener granted by both us or the LLC entity will immediately become fully vested.

Upon termination, Dr. Gottesdiener is entitled to reimbursement of his medical benefit premiums for so long as he is either entitled to severance under his letter agreement or otherwise becomes ineligible for COBRA, whichever is earlier.

Mr. Henderson. Under the terms of Mr. Henderson's letter agreement, upon termination without "cause," as defined below, or for "good reason," as defined below, subject to customary conditions, including his execution and nonrevocation of an acceptable release, Mr. Henderson will be entitled to receive a severance payment in an aggregate amount equal to six months of his base salary then in effect, paid in substantially equal installments over a period of six months in accordance with ordinary payroll practices.

Upon a termination without "cause" or for "good reason" within the three months immediately preceding or the 12 months immediately following a "sale of the company" as defined in his letter agreement, subject to customary conditions, including his execution and nonrevocation of an acceptable release. Mr. Henderson, in lieu of the above benefits, will be entitled to receive a severance payment in an aggregate amount equal to 12 months of his base salary then in effect, paid in substantially equal installments, over a period of 12 months in accordance with ordinary payroll practices, and a payment equal to 100% of his annual target bonus for the year in which the termination occurs. In addition, each unvested equity award held by Mr. Henderson granted by both us or the LLC entity will immediately become fully vested.

Upon termination, Mr. Henderson is entitled to reimbursement of his medical benefit premiums for so long as he is either entitled to severance under his letter agreement or otherwise becomes ineligible for COBRA, whichever is earlier.

On June 12, 2017, Mr. Henderson resigned his employment and entered into a consulting agreement with us to provide transition services.

Dr. Fidorek. Under the terms of Dr. Fidorek's letter agreement, upon termination without "cause," as defined below, or for "good reason," as defined below, subject to customary conditions, including his execution and nonrevocation of an acceptable release, Dr. Fidorek will be entitled to receive a severance payment in an aggregate amount equal to six months of his base salary then in effect, paid in substantially equal installments over a period of six months in accordance with ordinary payroll practices.

Upon a termination without "cause" or for "good reason" within the three months immediately preceding or the 12 months immediately following a "sale of the company" as defined in his letter agreement, subject to customary conditions, including his execution and nonrevocation of an acceptable release. Dr. Fidorek, in lieu of the above benefits, will be entitled to receive a severance payment in an aggregate amount equal to 12 months of his base salary then in effect, paid in substantially equal installments, over a period of 12 months in accordance with ordinary payroll practices, and a payment equal to 100% of his annual target bonus for the year in which the termination occurs. In addition, up to 50% of the unvested equity awards held by Dr. Fidorek granted by both us or the LLC entity will immediately become fully vested. However, if 50% or more of Dr. Fidorek's equity awards have already vested, there will be no further acceleration of vesting.

Upon termination, Dr. Fiedorek is entitled to reimbursement of his medical benefit premiums for so long as he is either entitled to severance under his letter agreement or otherwise becomes ineligible for COBRA, whichever is earlier.

For purposes of these letter agreements and those we intend to enter into with our named executive officers, "cause" generally means the occurrence of any of the following events by the individual: (i) commission of any crime involving fraud, breach of trust, or physical or emotional harm to any person, moral turpitude or dishonesty; (ii) any unauthorized use or disclosure of proprietary information (other than any such use or disclosure that is not intentional and is not material); (iii) any intentional misconduct or gross negligence that has a material adverse effect on business or reputation; (iv) any material breach by the executive of any agreement that is not cured within 30 days after receipt of notice; or (v) repeated and willful failure to perform the duties, functions and responsibilities of his position after a written warning from us.

For purposes of the letter agreements, "good reason" generally means resignation by the executive from all positions if, without the executive's written consent, there is a (i) material diminution of duties or authority; (ii) material reduction of the executive's base salary not pursuant to a program affecting all or substantially all employees unless the executive is affected to a greater extent than other similarly situated employees pursuant to such a program; or (iii) requirement to relocate the primary work location to a location that would increase the one way commute distance by more than 35 miles from the executive's primary work location as of immediately prior to such change, in each case, provided that the executive provides written notice within 30 days following such event, and failure to remedy the event within 30 days following receipt of such notice and the executive's resignation is effective no more than 30 days following the expiration of a cure period. Good reason may also occur if the executive resigns from all positions on the one year anniversary of a change in control if the executive has not entered into a written letter or agreement providing for the executive's continued employment with us or our successor.

Terms and Conditions of New Agreements with our Named Executive Officers

On September 13, 2017, our named executive officers, except for Bart Henderson who entered into a consulting agreement with us on June 12, 2017, entered into new letter agreements with us. The terms of the new letter agreements are substantially similar to the terms of the existing letter agreements described above under "—Agreements with our Named Executive Officers" except as set forth below, and will supersede in their entirety our named executive officers' prior employment agreements with us. These new agreements become effective upon the consummation of this offering.

Agreement with Dr. Gottesdiener. Under Dr. Gottesdiener's new letter agreement, he is entitled to a base salary of \$490,795, subject to adjustment in the committee's sole discretion, is eligible to receive an annual target performance bonus of up to 50% of his base salary, as determined by the committee, and is entitled to certain severance benefits, which, except as set forth below, are substantially similar to the terms in his November 2016 letter agreement which are described above under "—Potential Payments Upon Termination or Change of Control".

Upon Termination without "cause" or for "good reason" within the three months immediately preceding or the 12 months immediately following a "change of control" as defined in the letter agreement, subject to customary conditions, including his execution and nonrevocation of an acceptable release, Dr. Gottesdiener, in lieu of the above benefits, will be entitled to receive a severance payment in an aggregate amount equal to 12 months if the event occurs prior to our first underwritten public offering of common stock, or 18 months if such event occurs following our first underwritten public offering, of his base salary then in effect, paid in substantially equal installments over a period of 12 or 18 months, as applicable, in accordance with ordinary payroll practices, and a payment equal to 100% of his annual target bonus for the year in which the termination occurs. In addition, each unvested equity award held by Dr. Gottesdiener granted by both us or the LLC entity will immediately become fully vested.

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Agreement with Dr. Fiedorek. Under Dr. Fiedorek's new letter agreement, he is entitled to a base salary of \$354,732, subject to adjustment in the committee's sole discretion, is eligible to receive an annual target performance bonus of up to 30% of his base salary prior to our first underwritten public offering of common stock or 35% following this offering, as determined by the committee, and is entitled to certain severance benefits, which, except as set forth below, are substantially similar to the terms in his November 2016 letter agreement which are described above under "—Potential Payments Upon Termination or Change of Control".

Upon Termination without "cause" or for "good reason", within the three months immediately preceding or the 12 months immediately following a "change of control" as defined in the letter agreement, subject to customary conditions, including his execution and nonrevocation of an acceptable release, Dr. Fiedorek, in lieu of the above benefits, will be entitled to receive a severance payment in an aggregate amount equal to 12 months of his base salary then in effect, paid in substantially equal installments over a period of 12 months in accordance with ordinary payroll practices, and a payment equal to 100% of his annual target bonus for the year in which the termination occurs. In addition, each unvested equity award held by Dr. Fiedorek granted by us will immediately become fully vested.

Employee Benefit and Stock Plans

2017 Equity Incentive Plan

We have adopted the 2017 equity incentive plan which will be effective upon the closing of this offering, or the 2017 Plan. The following summary of the material terms of the 2017 Plan does not purport to be complete and is qualified by reference to the full text of the 2017 Plan, which we have filed as an exhibit to our registration statement of which this prospectus is a part.

The 2017 Plan provides for the grant of incentive stock options and nonstatutory stock options, stock appreciation rights, restricted stock and restricted stock unit awards, performance units, stock grants and qualified performance-based awards (that is, any of the foregoing that are intended to constitute performance-based compensation under Section 162(m) of the Code), which we collectively refer to as "awards" in connection with the 2017 Plan. Our directors, officers and other employees, as well as others performing consulting or advisory services for us, are eligible for grants under the Plan. The purpose of the Plan is to provide incentives that will attract, retain and motivate highly competent officers, directors, employees and consultants and advisors to promote the success of our business and align employees' interests with stockholders' interests. The 2017 Plan serves as the successor to our 2015 Plan, and no further awards will be made under the 2015 Plan following the closing of this offering. All awards outstanding under the 2015 Plan following the closing of this offering will be treated as outstanding under the 2017 Plan.

Administration

Under its terms, the 2017 Plan is administered by the compensation committee of our board of directors which is made up of independent outside non-employee directors for purposes of applicable securities and tax laws. The board of directors itself may also exercise any of the powers and responsibilities under the 2017 Plan. The compensation committee may delegate to an executive officer or officers the authority to grant awards under the 2017 Plan subject to applicable law and to guidelines specified by the compensation committee. Subject to the terms of the Plan, the compensation committee will select the recipients of awards and determine, among other things, the:

- number of shares of common stock covered by awards and the dates upon which such awards become exercisable or any restrictions to which they are subject lapse, as applicable;
- type of award and the exercise or purchase price and method of payment for each such award;

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- vesting period for awards, risks of forfeiture and any potential acceleration of vesting or lapses in risks of forfeiture; and
- duration of awards.

All decisions, determinations and interpretations made in good faith by the compensation committee with respect to the 2017 Plan and the terms and conditions of or operation of any award are final and binding on all participants, beneficiaries, heirs, assigns or other persons holding or claiming rights under the 2017 Plan or any award.

Available Shares

Subject to the following sentence, the aggregate number of shares of our common stock which may be issued under the 2017 Plan or with respect to which awards may be granted may not exceed 4,018,538 shares (including pursuant to incentive stock options), which may be either authorized and unissued shares of our common stock or shares of common stock held in or acquired for our treasury. The number of shares which may be issued under the 2017 Plan includes shares of our common stock available for issuance under the 2015 Plan as of the consummation of this offering, including the portion of those shares subject to options outstanding on that date. The number of shares authorized under the 2017 Plan will be increased each January 1, commencing on the first January 1 following consummation of our initial public offering, by an amount equal to 4% of outstanding shares of stock as of the end of the immediately preceding fiscal year. Notwithstanding the foregoing, our board of directors may act prior to January 1 of a given year to provide that there will be no such January 1 increase in the number of shares of stock authorized under the 2017 Plan for such year or that the increase in the number of shares of stock authorized under the 2017 Plan for such year will be a lesser number than would otherwise occur pursuant to the preceding sentence. Notwithstanding the preceding sentences, in no event shall the number of shares available for issuance pursuant to incentive options over the term of the 2017 Plan exceed 4,018,538 shares of stock. In general, if awards under the 2017 Plan are for any reason cancelled, or expire or terminate unexercised, the number of shares covered by such awards will again be available for the grant of awards under the 2017 Plan.

Eligibility for Participation

Members of our board of directors, as well as employees of, and consultants and advisors to, us or any of our subsidiaries and affiliates are eligible to receive awards under the 2017 Plan. The selection of participants is within the sole discretion of the compensation committee.

Individual Limitations

The maximum number of shares of common stock that may be subject to options or stock appreciation rights or any combination thereof granted to any one person during any single calendar year shall be 1,200,000. The maximum number of shares of common stock that may be subject to all other awards granted to any one person during any single calendar year that are intended to be qualified performance-based awards shall be 1,200,000. The maximum value of awards denominated in cash granted to any one person other than a non-employee member of our board of directors during any single calendar year and that are intended to be qualified performance-based awards shall be \$30,000,000. Each of the foregoing limitations shall be doubled with respect to awards granted to an individual during the first calendar year in which he or she commences employment. The maximum value of awards denominated in cash granted to any non-employee member of our board of directors during any single calendar year shall be \$1,000,000.

Incentive Stock Options

Incentive stock options are options that are intended to qualify as incentive stock options under Section 422 of the Code, and will be granted pursuant to incentive stock option agreements. Only our employees or employees of our parent or subsidiary corporations, as contemplated by the Code, are eligible to receive incentive stock options. The compensation committee will determine the exercise price for an incentive stock option, which may not be less than 100% of the fair market value of the stock underlying the option on the date of grant. In addition, incentive options granted to employees who own, or are deemed to own, more than 10% of our voting stock, must have an exercise price not less than 110% of the fair market value of the stock underlying the option on the date of grant. No incentive stock option may be exercised on or after the tenth anniversary of the date of grant, or after the fifth anniversary of the date of grant for employees who own, or are deemed to own, more than 10% of our voting stock.

Nonstatutory Stock Options

Nonstatutory stock options are not intended to qualify as incentive stock options under Section 422 of the Code and will be granted pursuant to nonstatutory stock option agreements. The compensation committee will determine the exercise price which may not be less than 100% of the fair market value of the stock underlying the option on the date of grant and term of a nonstatutory stock option.

Stock Appreciation Rights

A stock appreciation right, or a SAR, entitles a participant to receive a payment equal in value to the difference between the fair market value of a share of stock on the date of exercise of the SAR over a specified exercise price of the SAR. SARs may be granted in tandem with a stock option, such that the recipient has the opportunity to exercise either the stock option or the SAR, but not both. The exercise price (above which any appreciation is measured) will not be less than 100% of the fair market value of the common stock on the date of grant of the SAR or, in the case of an SAR granted in tandem with a stock option, the exercise price will be the same as the exercise price of the related stock option. The compensation committee may settle a SAR amount in cash, in shares of our common stock, or a combination of cash and shares of our common stock as determined by the compensation committee at or after grant but subject to the terms of the applicable award agreement. The terms, methods of exercise, and any other terms and conditions of any SAR will be determined by the compensation committee at the time of the grant of the award and will be reflected in the award agreement.

Restricted Stock and Restricted Stock Units

A restricted stock award or restricted stock unit award is the grant of shares of our common stock either currently (in the case of restricted stock) or at a future date (in the case of restricted stock units) at a price determined by the compensation committee (including zero), based on satisfaction of certain vesting conditions, including continuing employment or other service, or achievement of performance goals. During the vesting period, participants holding shares of restricted stock shall, except as otherwise provided in the Plan or an individual award agreement, have full voting and dividend rights with respect to such shares but any stock dividends or other distributions payable in shares of stock or other securities of ours will be subject to the same vesting conditions that apply to the shares of restricted stock in respect of which the dividend was made. The receipt of cash dividends may also be deferred or required to be invested in additional shares of restricted stock. Participants holding restricted stock units may be entitled to receive payments equivalent to any dividends declared with respect to the common stock referenced in the grant of the restricted stock units, but only following the close of the applicable restriction period and then only if the employment or other service and/or performance goals have been met. The restrictions will lapse in accordance with a schedule or other conditions determined by the compensation committee. The compensation committee may settle restricted stock units in cash, in shares of our common stock, or a

combination of cash and shares of our common stock as determined by the compensation committee at or after grant but subject to the terms of the applicable award agreement.

Performance Units

A performance unit award is a contingent right to receive the value of a specified number of shares of our common stock over an initial value for such number of shares (which may be zero) established by the compensation committee at the time of grant if certain performance goals or other business objectives are met with the specified performance period. The value of performance units will depend on the degree to which the specified performance goals are achieved. The compensation committee may, in its discretion, pay earned performance units in cash, in shares of our common stock, or a combination of both cash and shares of our common stock as determined by the compensation committee at or after grant but subject to the terms of the applicable award agreement.

The compensation committee has discretion to select the length of any applicable restriction or performance period, the kind and/or level of the applicable performance goal and whether the performance goal is to apply to us, to one of our subsidiaries or any division or business unit or to the recipient.

Stock Grants

A stock grant is an award of shares of common stock without restriction. Stock grants may only be made in limited circumstances, such as in lieu of other earned compensation or as an inducement to employment. Stock grants are made without any forfeiture conditions.

Qualified Performance-Based Awards

Qualified performance-based awards are earned based on the achievement of certain performance criteria intended to satisfy Section 162(m) of the Code. Section 162(m) of the Code limits our federal income tax deduction for compensation to certain of our executive officers to \$1.0 million dollars, but excludes from that limit "performance-based compensation." Any form of award permitted under the 2017 Plan other than a stock grant may be granted as a qualified performance-based award, but, in the case of awards other than stock options and SARs, will be subject to satisfaction of pre-established, objective performance goals. Qualified performance-based awards include any of the foregoing awards that are granted subject to vesting and/or payment based on the attainment of specified performance goals. Performance criteria upon which performance goals are established by the plan administrator may include but are not limited to: (i) net earnings (either before or after one or more of (A) interest, (B) taxes, (C) depreciation and (D) amortization); (ii) gross or net sales or revenue; (iii) net income (either before or after taxes); (iv) adjusted net income; (v) operating earnings or profit; (vi) cash flow (including, but not limited to, operating cash flow and free cash flow); (vii) return on assets; (viii) return on capital; (ix) return on stockholders' equity; (x) total stockholder return; (xi) return on sales; (xii) gross or net profit or operating margin; (xiii) costs; (xiv) expenses; (xv) working capital; (xvi) earnings per share; (xvii) adjusted earnings per share; (xviii) price per share; (xix) regulatory body approval for commercialization of a product; (xx) implementation, completion or attainment of objectives relating to research, development, regulatory, commercial or strategic milestones or developments; (xxi) market share; (xxii) economic value; (xxiii) revenue; (xxiv) revenue growth; and (xxv) operational and organizational metrics.

Transferability

Awards, other than stock grants, granted under the 2017 Plan are generally nontransferable (other than by will or the laws of descent and distribution), except that the compensation committee may, at the time of grant or thereafter, provide for the transferability of nonstatutory stock options or restricted stock

to certain family members and/or certain trusts, foundations or other entities owned or controlled by such family members.

Adjustment for Corporate Actions

In the event of any change in the outstanding shares of common stock as a result of a reorganization, recapitalization, reclassification, stock dividend, stock split, reverse stock split or other similar distribution with respect to the shares of common stock, an equitable adjustment will be made in (i) the maximum numbers and kinds of shares subject to the 2017 Plan, (ii) the numbers and kinds of shares or other securities subject to then outstanding awards, (iii) the exercise price for each share or unit of any other securities subject to then outstanding stock options or SARs (without change in the aggregate purchase price as to which such stock options or SARs remain exercisable), and (iv) the repurchase price of each share of restricted stock then subject to a risk of forfeiture in the form of a company repurchase right. Any such adjustment in awards will be determined and made by the compensation committee in its sole discretion.

Transactions

In the event of a transaction, including (i) any merger or consolidation of our company with or into another entity as a result of which our stock is converted into or exchanged for the right to receive cash, securities or other property or is cancelled, (ii) any sale or exchange of all or substantially all of our common stock for cash, securities, or other property, (iii) any sale, transfer or other disposition of all or substantially all of our assets to one or more other persons in a single transaction or series of related transactions, or (iv) any liquidation or dissolution of our company, the compensation committee may, (1) provide that awards will be assumed, or substantially equivalent rights shall be provided in substitution therefor by the acquiring or succeeding entity (or an affiliate thereof), (2) upon written notice to the recipient, provide that the recipient's unexercised outstanding stock options and SARs will terminate immediately prior to the consummation of such transaction unless exercised within a specified period following the date of such written notice, (3) provide that all or any unvested restricted stock or restricted stock unit awards will terminate immediately prior to the consummation of such transaction, (4) provide that all or any outstanding stock options and SARs shall become exercisable in whole or in part prior to or upon the transaction, (5) provide that the vesting of all or any unrestricted stock or restricted stock unit awards shall accelerate and any restrictions applicable to such awards shall lapse prior to or upon such transaction, (6) provide for cash payments, net of applicable tax withholdings, to be made to the recipients, (7) provide that, in connection with our liquidation or dissolution, awards other than awards of restricted stock or stock grants shall convert into the right to receive liquidation proceeds net of the exercise price of the awards and any applicable tax withholdings, or (8) any combination of the foregoing. With respect to outstanding awards other than stock options or SARs, that are not terminated prior to or upon the transaction, upon the occurrence of a transaction other than our liquidation or dissolution which is not part of another form of transaction, our repurchase and other rights under each such award will transfer to our successor and inure to the benefit of our successor, and shall, unless the compensation committee determines otherwise, apply to the cash, securities or other property which the stock was converted into or exchanged for pursuant to such transaction in the same manner and to the same extent as they applied to the award. In taking any of the actions described in the event of a transaction, the compensation committee is not obligated to treat all awards, all awards held by a participant or all awards of the same type identically.

Change of Control

Except as otherwise provided in the 2017 Plan or in the applicable award agreement, in the event of a change of control, to the extent that the surviving entity declines to continue, convert, assume or replace

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outstanding awards, then all such awards shall become fully vested and exercisable and any restrictions applicable to any such awards shall lapse in connection with the transaction.

A change of control is defined as the occurrence of any of the following: (1) a transaction, as described above, unless securities possessing more than 50% of the total combined voting power of the resulting entity or acquiror's outstanding securities (or the securities of any parent thereof) are held by a person or persons who held securities possessing more than 50% of the total combined voting power of our outstanding securities immediately prior to the transaction; (2) any person or group of persons, excluding our company and certain other related entities or any of its affiliates, directly or indirectly acquires, including but not limited to by means of a merger or consolidation, beneficial ownership of securities possessing more than 50% of the total combined voting power of our outstanding securities, unless pursuant to a tender or exchange offer made directly to our stockholders that our board of directors recommends such stockholders accept; or (3) over a period of no more than 36 consecutive months there is a change in the composition of our board such that a majority of the board members ceases to be composed of individuals who either (i) have been board members continuously since the beginning of that period, or (ii) have been elected or nominated for election as board members during such period by at least a majority of the remaining board members who have been board members continuously since the beginning of that period; or (4) a majority of the board of directors votes in favor of a decision that a change of control has occurred.

Amendment and Termination

Our board of directors may at any time amend any or all of the provisions of the 2017 Plan, or suspend or terminate it entirely, retroactively or otherwise. However, except as set forth in the Plan, we must obtain stockholder approval to increase the number of shares available under the Plan, or to change the description of persons eligible for awards, or as otherwise required by law or applicable stock exchange rules. Unless otherwise required by law or specifically provided in the Plan, the rights of a participant under awards granted prior to any amendment, suspension or termination may not be adversely affected without the consent of the participant. Unless the 2017 Plan is earlier terminated by our board of directors, the Plan terminates immediately prior to the tenth anniversary of the effective date.

Allocation of Awards; Plan Benefits.

It is not presently possible to determine the dollar value of award payments that may be made or the number of options, shares of restricted stock, restricted stock units, or other awards that may be granted under the 2017 Plan in the future, or the individuals who may be selected to receive such awards because awards under the 2017 Plan are granted at the discretion of the compensation committee.

2015 Equity Incentive Plan

The 2015 Equity Incentive Plan, or the 2015 Plan was adopted on August 3, 2015, and was amended on January 5, 2017 to increase the number of shares issuable under the 2015 Plan. The following summary of the 2015 Plan does not purport to be complete and is qualified by reference to the full text of the 2015 Plan which we have filed as an exhibit to our registration statement of which this prospectus is a part. Following this offering and in connection with the effectiveness of our 2017 Plan, the 2015 Plan will terminate and no further awards will be granted under the 2015 Plan. All awards outstanding under the 2015 Plan will be transferred to the 2017 Plan and will be treated as outstanding under the 2017 Plan. However, each such transferred award will continue to be governed by its existing terms.

The 2015 Plan provides for the grant of incentive stock options and nonstatutory stock options, restricted stock awards and stock grants, which we collectively refer to as "awards" in connection with the 2017 Plan. Our directors, officers and other employees, as well as consultants are eligible to receive grants under the 2015 Plan. The purpose of the 2015 Plan is to encourage ownership of our common stock by

employees, consultants, officers and directors and to provide additional incentive to them to promote the success of our business.

Administration

Under its terms, the 2015 Plan is administered by the compensation committee of our board of directors which is made up of independent outside non-employee directors for purposes of applicable securities and tax laws. The board of directors itself may also exercise any of the powers and responsibilities under the 2015 Plan. The compensation committee may delegate to an executive officer or officers the authority to grant awards under the 2015 Plan subject to applicable law and to guidelines specified by the compensation committee. Subject to the terms of the 2015 Plan, the compensation committee will select the recipients of awards and determine, among other things, the:

- recipient of an award;
- form of award and the exercise or purchase price and method of payment for each such award;
- vesting period for awards, risks of forfeiture and any potential acceleration of vesting or lapses in risks of forfeiture; and
- duration of awards.

All determinations made in good faith by the compensation committee with respect to the 2015 Plan and the terms and conditions of or operation of any award are final and binding on all participants, beneficiaries, heirs, assigns or other persons holding or claiming rights under the 2015 Plan or any award.

Available Shares

The aggregate number of shares of our common stock which may be issued under the 2015 Plan or with respect to which awards may be granted may not exceed 2,317,339 shares (including pursuant to incentive stock options), which may be either authorized and unissued shares of our common stock or shares of common stock held in or acquired for our treasury. In general, if awards under the 2015 Plan are for any reason cancelled, or expire or terminate unexercised, the number of shares covered by such awards will again be available for the grant of awards under the 2015 Plan.

Eligibility for Participation

Members of our board of directors, as well as employees of, and consultants to, us or any of our subsidiaries and affiliates are eligible to receive awards under the 2015 Plan. The selection of participants is within the sole discretion of the compensation committee.

Stock Options

The 2015 Plan provides for the grant of nonstatutory stock options and incentive stock options. Incentive stock options may only be granted to employees. The exercise price of an incentive stock option must be at least 100% of the fair market value of the common stock on the grant date, or 110% for employees who own or are deemed to own more than 10% of our voting stock. No incentive stock option may be exercised on or after the tenth anniversary or the grant date or after the fifth anniversary of the grant date for employees who own or are deemed to own more than 10% of our voting stock. Stock options generally are not transferable except by will or the laws of descent and distribution.

Restricted Stock

A restricted stock award is the grant of shares of our common stock at a price determined by the compensation committee (including zero), based on satisfaction of certain vesting conditions, including continuing employment or other service, or achievement of performance goals. During the vesting period,

participants holding shares of restricted stock shall, except as otherwise provided in the 2015 Plan or an individual award agreement, have full voting rights with respect to such shares. In general, restricted stock may not be sold, transferred, pledged, assigned or otherwise alienated or hypothecated until the restrictions have lapsed or are removed. The restrictions lapse in accordance with a schedule or other conditions determined by the compensation committee.

Stock Grants

A stock grant is an award of shares of common stock without restriction for such consideration, in cash, other property or services or any combination thereof, as is determined by the committee. Stock grants may be awarded in such circumstances as the committee deems appropriate, including in recognition of significant contributions to our success or in lieu of compensation already due.

Adjustment for Corporate Actions

In the event of any change in the outstanding shares of common stock as a result of a reorganization, recapitalization, reclassification, stock dividend, stock split, reverse stock split or other similar distribution with respect to the shares of common stock, an appropriate and proportionate adjustment will be made in (i) the maximum numbers and kinds of shares subject to the 2015 Plan, (ii) the numbers and kinds of shares or other securities subject to then outstanding awards, (iii) the exercise price for each share subject to then outstanding stock options, and (iv) the repurchase price of each share of restricted stock then subject to a risk of forfeiture in the form of a company repurchase right. Any such adjustment in awards will be determined and made by the compensation committee in its sole discretion.

Change of Control

Except as otherwise provided in the 2015 Plan or in the applicable award agreement, in the event of a change of control, the committee has the discretion to determine the treatment of each outstanding award and may provide that the awards will be assumed or substituted, that the awards will terminate or accelerate in full immediately prior to the change in control, or that awards will terminate in exchange for cash or other property.

Amendment and Termination

Our board of directors may at any time terminate or amend the 2015 Plan as it deems advisable. Following this offering and in connection with the effectiveness of our 2017 Plan, the 2015 Plan will terminate and no further awards will be granted under it.

2017 Employee Stock Purchase Plan

We expect our board of directors to adopt and our stockholders to approve the 2017 employee stock purchase plan, or the ESPP, which will become effective immediately prior to the completion of this offering. The following summary of the material terms of the ESPP does not purport to be complete and is qualified by reference to the full text of the ESPP, which is filed as an exhibit to our registration statement of which this prospectus is a part.

The ESPP provides an incentive to, and encourages stock ownership by, all of our eligible employees and those of our participating subsidiaries so that they may share in our growth by acquiring or increasing their share ownership in us. It is intended that the ESPP constitute an "employee stock purchase plan" within the meaning of Section 423 of the Code. Under the ESPP, eligible employees may purchase shares of our common stock at a discount through payroll deductions.

Administration

The ESPP is administered by the compensation committee of our board of directors. The board of directors itself may exercise any of the powers and responsibilities under the ESPP. The compensation committee may delegate its duties in order to facilitate the purchase and transfer of shares of our common stock and for the day-to-day administration of the ESPP. The compensation committee, has the discretion, subject to the provisions of the ESPP, to make or to select the manner of making all determinations with respect to options granted under the ESPP. Further, the compensation committee has complete authority to interpret the ESPP, to prescribe, amend and rescind rules and regulations relating to it, and to make all other determinations necessary or advisable for the administration of the ESPP. All decisions, determinations and interpretations made in good faith by the compensation committee with respect to the ESPP are final and binding on all persons having or claiming any interest in the ESPP or any option granted under the ESPP.

Shares Subject to the Plan

The shares issued or to be issued under the ESPP are authorized but unissued shares of our common stock or are shares held by us in our treasury. Subject to the following sentence, the ESPP authorizes the issuance of up to 258,433 shares of common stock. The number of shares authorized under the ESPP will be increased each January 1, commencing on the first January 1 following consummation of our initial public offering and ending on (and including) January 1, 2027, by an amount equal to the lesser of 1% of outstanding shares as of the end of the immediately preceding fiscal year and 646,083. Notwithstanding the foregoing, our board of directors may act prior to January 1 of a given year to provide that there will be no such January 1 increase in the number of shares authorized under the ESPP for such year, or that the increase in the number of shares authorized under the ESPP for such year will be a lesser number than would otherwise occur pursuant to the preceding sentence.

Terms of Participation

The ESPP will be implemented through a series of purchase periods called "plan periods." The initial plan period shall commence on May 1 or November 1 of the calendar year as the Committee may determine, and will continue for six months. After the initial plan period, there will be two consecutive six-month plan periods, during each twelve month period thereafter, beginning on May 1 and ending on the immediately following October 31, and beginning on November 1 and ending on the immediately following April 30 unless otherwise determined by the compensation committee. An eligible employee will be granted an option at the beginning of the plan period, and can accumulate money to pay the exercise price for the option by electing to have payroll deductions taken from each payroll during a plan period of an amount, in whole percentages, between 1% and 15% of his or her compensation, but will not exceed \$25,000 on an annual basis. At the end of each plan period, unless the participating employee has withdrawn from the ESPP, the option will be exercised by applying the employee's accumulated payroll deductions to the purchase of shares of our common stock. The exercise price paid by the employee will be the lower of 85% of the fair market value of our common stock at (i) the commencement of the plan period and (ii) the end of the plan period.

Withdrawal

An employee may withdraw from participation in an offering up to two weeks prior to the plan period termination date and permanently draw out the balance accumulated in his or her account. In such case, the employee's option for the plan period he or she is withdrawing from will be automatically terminated. A participant's withdrawal from a plan period will not have any effect upon his or her eligibility to participate in a succeeding plan period or in any similar plan which we may adopt. If a participant's employment ends prior to a plan period termination date for any reason, including retirement or death, the

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contributions credited to his or her account will be returned to him or her or, in the case of his or her death, to his or her designated beneficiaries, and his or her option will be automatically terminated.

Eligibility

Our employees and those of a participating subsidiary are eligible to participate in the ESPP if we customarily employ them for at least 20 hours per week and more than five months per year, provided that the compensation committee may waive one or both requirements prior to the start of a plan period. However, no employee shall be granted an option under the ESPP if, immediately after the grant, the employee would own stock, including any outstanding options to purchase stock, equaling 5% or more of the total voting power or value of all classes of our stock. In addition, the ESPP provides that no employee may be granted an option if the option would permit the employee to purchase stock under all of our employee stock purchase plans in an amount that exceeds \$25,000 of the fair market value of such stock, determined as of the date(s) of grant, for each calendar year in which the option is outstanding.

Adjustment for Corporate Actions

In the event of any change in the outstanding shares of common stock as a result of a reorganization, recapitalization, reclassification, stock dividend, stock split, reverse stock split, or other similar distribution with respect to the shares of common stock, an appropriate and proportionate adjustment will be made in (i) the maximum numbers and kinds of shares subject to the ESPP, (ii) the numbers and kinds of shares or other securities subject to the then outstanding options, and (iii) the exercise price for each share or other unit of any other securities subject to then outstanding options.

Corporate Transactions

In the event of our dissolution or liquidation, the plan period then in progress will terminate unless otherwise provided by the compensation committee. In the event of another significant corporate transaction such as a merger or consolidation of us with and into another person or entity or the sale or transfer of all or substantially all of our assets, each right to purchase stock under the ESPP may be assumed, or an equivalent right substituted by, the successor corporation or a parent or subsidiary of the successor corporation. In the event that the successor corporation refuses to assume each purchase right or to substitute an equivalent right, any ongoing offering period will be shortened so that employees' rights to purchase stock under the ESPP are exercised prior to the transaction, unless the employee has withdrawn.

Amendment and Termination

Our board of directors has the power to amend or terminate the ESPP and to change or terminate plan periods as long as any such action does not adversely affect any outstanding rights to purchase stock; provided, however, that the board of directors may amend or terminate the ESPP or a plan period even if it would adversely affect outstanding options in order to avoid our incurring adverse accounting charges or if the board of directors determines that termination of the ESPP and/or plan period is in our best interest and the best interest of our stockholders. The ESPP will continue in effect until the tenth anniversary of the closing of the offering described in this prospectus, unless earlier terminated by the board of directors.

Amount of Benefits

The dollar value of benefits that will be received by any employee or group of employees in the ESPP is not determinable due to the voluntary nature of the ESPP and the variables involved in the calculation of any such benefits (including our stock price).

401(k) Plan

We maintain a tax-qualified retirement plan that provides eligible U.S. employees with an opportunity to save for retirement on a tax advantaged basis. Eligible employees are able to defer eligible compensation up to certain Code limits, which are updated annually. We have the ability to make matching and discretionary contributions to the 401(k) plan but have not done so to date. Employee contributions are allocated to each participant's individual account and are then invested in selected investment alternatives according to the participants' directions. Employees are immediately and fully vested in their own contributions. The 401(k) plan is intended to be qualified under Section 401(a) of the Code, with the related trust intended to be tax exempt under Section 501(a) of the Code. As a tax-qualified retirement plan, contributions to the 401(k) plan are deductible by us when made, and contributions and earnings on those amounts are not taxable to the employees until withdrawn or distributed from the 401(k) plan.

Non-Employee Director Compensation

The following table sets forth the compensation we paid to our non—employee directors during 2016. Other than as set forth in the table below, we did not pay any compensation, make any equity awards or non-equity awards to, or pay any other compensation to any non-employee directors in 2016.

Prior to this offering, we did not have a formal policy for compensating our non-employee directors but the board determined to pay our outside directors cash and equity awards in 2016 as compensation for their services. However, non-employee directors may receive stock options and other equity awards under the Plan from time to time as determined by our board of directors. We also reimburse non-employee directors for travel expenses incurred in connection with their duties as directors.

Name	Fees Earned or Paid in Cash (\$)	Option Awards Compensation (\$) ⁽¹⁾	Total (\$)
Neil Exter	—	—	—
Todd Foley	—	—	—
Christophe R. Jean	—	—	—
David W. J. McGirr	\$ 25,000	180,000	\$ 205,000
David P. Meeker	\$ 12,500	180,000	\$ 192,500
Ed Mathers	—	—	—
Jonathan T. Silverstein, J.D.	—	—	—

(1) As of December 31, 2016, David McGirr and David Meeker each had 65,430 outstanding options, 21,810 of which were vested options and 43,620 of which were unvested options. The aggregate grant date fair value was \$2.75.

In August 2017, our board of directors adopted a non-employee director compensation policy that will be effective upon completion of this offering. We retained an independent compensation consultant to help us determine the terms of the non-employee director compensation policy. Our non-employee director compensation policy is designed to provide a total compensation package that enables us to attract and retain, on a long-term basis, skilled non-employee directors. Under the policy, all non-employee

directors will be paid an annual retainer fee of \$35,000 and such additional fees as are set forth in the following table. All payments will be made quarterly in arrears.

<u>Non-Employee Director</u>	<u>Annual Fee</u>
Lead Director	\$ 25,000
Non-Executive Chair	\$ 30,000
Chairman of the audit committee	\$ 15,000
Member of the audit committee (other than chairman)	\$ 7,500
Chairman of the compensation committee	\$ 10,000
Member of the compensation committee (other than chairman)	\$ 5,000
Chairman of the governance and nominating committee	\$ 8,000
Member of the governance and nominating committee (other than chairman)	\$ 4,000

Under the non-employee director compensation policy, each individual who is initially appointed or elected to the board of directors will be eligible to receive an option to purchase up to 20,000 shares of our common stock under the Plan on the date he or she first becomes a nonemployee director. These option grants will vest annually over a three-year period from the date of grant, subject to continued service as a non-employee director through that vesting date. In addition, on the date of the annual meeting of stockholders, each continuing non-employee director who has served on the board of directors for a minimum of six months will be eligible to receive an option grant to purchase up to 10,000 shares of our common stock, which will vest in full upon the earlier of the first anniversary of the date of grant or the date of the next annual meeting of stockholders. The exercise price for each of these option grants will be equal to the fair market value of our common stock on the date of grant. These new director grants and annual grants will be subject to approval by our board of directors at the time of grant.

Limitation on Liability and Indemnification Matters

Section 145 of the Delaware General Corporation Law authorizes a corporation's board of directors to grant, and authorizes a court to award, indemnity to officers, directors and other corporate agents.

As permitted by Delaware law, our amended and restated certificate of incorporation provides that, to the fullest extent permitted by Delaware law, no director will be personally liable to us or our stockholders for monetary damages for breach of fiduciary duty as a director. Pursuant to Delaware law, such protection would be not available for liability:

- for any breach of a duty of loyalty to us or our stockholders;
- for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- for any transaction from which the director derived an improper benefit; or
- for an act or omission for which the liability of a director is expressly provided by an applicable statute, including unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law.

Our amended and restated certificate of incorporation also provides that if Delaware law is amended after the approval by our stockholders of the amended and restated certificate of incorporation to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law.

Our amended and restated bylaws further provide that we must indemnify our directors and officers to the fullest extent permitted by Delaware law. Our amended and restated bylaws also authorize us to indemnify any of our employees or agents and permit us to secure insurance on behalf of any officer,

director, employee or agent for any liability arising out of his or her action in that capacity, whether or not Delaware law would otherwise permit indemnification.

In addition, our amended and restated bylaws provide that we are required to advance expenses to our directors and officers as incurred in connection with legal proceedings against them for which they may be indemnified and that the rights conferred in the amended and restated bylaws are not exclusive.

We intend to enter into indemnification agreements with each of our directors and executive officers. These agreements, among other things, would require us to indemnify each director and officer to the fullest extent permitted by Delaware law, the amended and restated certificate of incorporation and amended and restated bylaws, for expenses such as, among other things, attorneys' fees, judgments, fines and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action by or in our right, arising out of the person's services as our director or executive officer or as the director or executive officer of any subsidiary of ours or any other company or enterprise to which the person provides services at our request. Upon consummation of the offering, we intend to obtain and maintain directors' and officers' liability insurance.

The SEC has taken the position that personal liability of directors for violation of the federal securities laws cannot be limited and that indemnification by us for any such violation is unenforceable. The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against our directors and officers for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and other stockholders. Further, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement and damage awards against directors and officers as required by these indemnification provisions.

Rule 10b5-1 Sales Plans

Our directors and executive officers may adopt written plans, known as Rule 10b5-1 plans, pursuant to which, if adopted, they would contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from them. The director or officer may amend a Rule 10b5-1 plan in some circumstances and may terminate a plan at any time. Our directors and executive officers also may buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material nonpublic information subject to compliance with the terms of our insider trading policy. Prior to 180 days after the date of this offering (subject to early termination), the sale of any shares under such plan would be subject to the lock-up agreement that the director or officer has entered into with the underwriters.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

We describe below transactions and series of similar transactions, during our last three fiscal years, to which we were a party or will be a party, in which:

- the amounts involved exceeded or will exceed \$120,000; and
- any of the directors, executive officers or holders of more than 5% of our voting equity, or any member of the immediate family of the foregoing persons, had or will have a direct or indirect material interest.

Compensation arrangements for our directors and named executive officers are described elsewhere in this prospectus.

Series A Preferred Stock Financing

In August 2015 and December 2015, pursuant to the series A preferred stock purchase agreement we issued an aggregate of 40,000,000 shares of series A preferred stock, par value \$0.001 per share, at a purchase price of \$1.00 per share, resulting in aggregate gross proceeds of \$40.0 million to us.

In January 2017 and August 2017, pursuant to the series A preferred stock purchase agreement we issued an aggregate of 40,949,999 shares of series A preferred stock, par value \$0.001 per share, at a purchase price of \$1.00 per share, resulting in aggregate gross proceeds of \$40.9 million to us.

Following the closing of this offering and upon the expiration of the lock-up period, holders of our series A preferred stock will be entitled to certain registration rights with respect to the resale of such shares under the Securities Act, pursuant to the investors' rights agreement entered into between us and certain of our stockholders. See "Description of Capital Stock—Registration Rights."

The following table summarizes the participation in the series A preferred stock financing by our directors, executive officers, holders of more than 5% of our voting securities, or any member of the

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immediate family of the foregoing persons. For further information on the ownership of securities of holders of more than 5% of our voting securities, see "Principal Stockholders."

Name	Shares of Series A Preferred Stock	Date(s) Purchased
OrbiMed Private Investments V, LP	10,937,500	August 3, 2015
667 L.P. and Baker Brothers Life Sciences, L.P.	5,000,000	August 3, 2015
New Enterprise Associates 13, L.P.	1,706,250	August 3, 2015
MPM BioVentures V, L.P. and MPM Asset Management Investors BV5 LLC	1,012,500	August 3, 2015
Pfizer Inc.	550,000	August 3, 2015
Third Rock Ventures, L.P.	143,750	August 3, 2015
OrbiMed Private Investments V, LP	6,562,500	December 1, 2015
667 L.P. and Baker Brothers Life Sciences, L.P.	3,000,000	December 1, 2015
New Enterprise Associates 13, L.P.	1,023,750	December 1, 2015
MPM BioVentures V, L.P. and MPM Asset Management Investors BV5 LLC	607,500	December 1, 2015
Pfizer Inc.	330,000	December 1, 2015
Third Rock Ventures, L.P.	86,250	December 1, 2015
New Enterprise Associates 13, L.P.	5,067,162	January 6, 2017
Third Rock Ventures, L.P.	4,624,751	January 6, 2017
MPM BioVentures V, L.P. and MPM Asset Management Investors BV5 LLC	3,015,916	January 6, 2017
OrbiMed Private Investments V, LP	2,924,766	January 6, 2017
Pfizer Inc.	1,611,852	January 6, 2017
667 L.P. and Baker Brothers Life Sciences, L.P.	1,337,036	January 6, 2017
David P. Meeker	250,000	January 6, 2017
Keith M. Gottesdiener, M.D.	125,000	January 6, 2017
Bart Henderson	100,000	January 6, 2017
New Enterprise Associates 13, L.P.	5,067,162	August 18, 2017
Third Rock Ventures, L.P.	4,624,751	August 18, 2017
MPM BioVentures V, L.P. and MPM Asset Management Investors BV5 LLC	3,015,915	August 18, 2017
OrbiMed Private Investments V, LP	2,924,765	August 18, 2017
Pfizer Inc.	1,611,852	August 18, 2017
667 L.P. and Baker Brothers Life Sciences, L.P.	1,337,035	August 18, 2017
David P. Meeker	250,000	August 18, 2017
Keith M. Gottesdiener, M.D.	125,000	August 18, 2017
Bart Henderson	100,000	August 18, 2017

Certain of our existing principal stockholders, directors and their affiliated entities, have indicated an interest in purchasing an aggregate of approximately \$40.0 million in shares of our common stock in this offering at the initial public offering price per share and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers, and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering.

Indemnification Agreements

We currently have an indemnification agreement with Jonathan T. Silverstein. Upon the completion of this offering, we intend to enter into new indemnification agreements with each of our directors and executive officers. These agreements, among other things, will require us to indemnify each director and officer to the fullest extent permitted by Delaware law, our amended and restated certificate of incorporation and amended and restated bylaws, for expenses such as, among other things, attorneys' fees, judgments, fines, and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action by or in our right, arising out of the person's services as our director or executive officer or as the director or executive officer of any subsidiary of ours or any other company or enterprise to which the person provides services at our request. Upon consummation of the offering, we intend to obtain and maintain directors' and officers' liability insurance. See "Executive and Director Compensation—Limitation on Liability and Indemnification Matters."

Employment and Board Arrangements

Our executive officers have employment letters with us for their services. For information about the employment letters with our named executive officers, refer to "Executive and Director Compensation—Agreements with our Executive Officers."

Transactions with Baker Bros. Advisors LP

The board of directors has invited Sara Brownstein of Baker Bros. Advisors LP to continue to participate in meetings of the board of directors in a non-voting observer capacity. See "Management—Board Observer Rights."

Consulting Agreement with Mr. Henderson

Mr. Henderson resigned from employment with us and thereafter entered into a consulting agreement with us. Under the terms of Mr. Henderson's consulting agreement, he is entitled to a consulting fee on an hourly basis, subject to adjustment by us. In consideration of Mr. Henderson's prior service to us as a founder and former officer and employee, under the terms of Mr. Henderson's consulting agreement with us, Mr. Henderson will continue to vest in any unvested equity awards held by him granted by both us or the LLC entity, through and including December 31, 2017, with a right to exercise any vested equity through and including October 1, 2018.

Related Party Transactions Policy

Our board of directors has adopted a policy, effective upon the closing of this offering, that our executive officers, directors, nominees for election as a director, beneficial owners of more than 5% of any class of our common stock and any members of the immediate family of any of the foregoing persons are not permitted to enter into a related person transaction with us without the prior review and approval of our governance and nominating committee. Any request for us to enter into a transaction with an executive officer, director, nominee for election as a director, beneficial owner of more than 5% of any class of our common stock or any member of the immediate family of any of the foregoing persons in which the amount involved exceeds \$120,000 and such person would have a direct or indirect material interest must first be presented to our governance and nominating committee for review, consideration and approval. In approving or rejecting any such proposal, our governance and nominating committee is to consider the material facts of the transaction, including, but not limited to, whether the transaction is on terms no less favorable than terms generally available to an unaffiliated third party under the same or similar circumstances and the extent of the related person's interest in the transaction. We did not have a formal review and approval policy for related party transactions at the time of any of the transactions described above. However, the transactions described above under "Certain Relationships and Related Party Transactions" were entered into after presentation, consideration and approval by our board of directors.

PRINCIPAL STOCKHOLDERS

The following table sets forth information regarding the beneficial ownership of our common stock as of September 22, 2017, after giving effect to the conversion of our outstanding shares of preferred stock into shares of common stock, by:

- each of our directors and named executive officers;
- all of our directors and executive officers as a group; and
- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock.

Beneficial ownership is determined according to the rules of the SEC and generally means that a person has beneficial ownership of a security if he, she or it possesses sole or shared voting or investment power of that security, and of convertible securities that are currently exercisable or exercisable within 60 days after September 22, 2017. Shares of our common stock issuable pursuant to options or warrants, if any, are deemed outstanding for computing the percentage of the person holding such options or warrants and the percentage of any group of which the person is a member but are not deemed outstanding for computing the percentage of any other person. Except as indicated by the footnotes below, we believe, based on the information furnished to us, that the persons named in the table below have sole voting and investment power with respect to all shares of common stock shown that they beneficially own, subject to community property laws where applicable. The information does not necessarily indicate beneficial ownership for any other purpose, including for purposes of Section 13(d) and 13(g) of the Securities Act.

Our calculation of the percentage of beneficial ownership prior to this offering is based on 19,176,640 shares of common stock outstanding as of September 22, 2017, assuming the conversion of our outstanding preferred stock into common stock, as if the conversion had occurred as of September 22, 2017. Our calculation of the percentage of beneficial ownership after this offering is based on 25,843,306 shares of common stock outstanding immediately after the closing of this offering (assuming no exercise of the underwriters' option to purchase additional shares of our common stock).

Certain of our existing principal stockholders, directors and their affiliated entities, have indicated an interest in purchasing an aggregate of approximately \$40.0 million in shares of our common stock in this offering at the initial public offering price per share and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers, and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering. The following table does not reflect any potential purchases by these potential purchasers. If any shares are purchased by our existing principal stockholders, directors or their affiliated entities, the number and percentage of shares of our common stock beneficially owned by them after this offering will differ from those set forth in the following table.

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Except as otherwise noted below, the address for persons listed in the table is c/o Rhythm Pharmaceuticals, Inc., 500 Boylston Street, Eleventh Floor, Boston, MA 02116.

Name and Address of Beneficial Owner	Prior to the Offering		After the Offering	
	Number of shares of common stock	Percent of class	Number of shares of common stock	Percent of class
5% Stockholders:				
New Enterprise Associates 13, L.P. and NEA Ventures 2009 Limited Partnership ⁽¹⁾ 2855 Sand Hill Road Menlo Park, CA 94025	4,362,306	22.75%	4,362,306	16.88%
Third Rock Ventures, L.P. ⁽²⁾ 29 Newbury Street Boston, MA 02116	3,981,437	20.76%	3,981,437	15.41%
MPM BioVentures V, L.P. and MPM Asset Management Investors BV5 LLC ⁽³⁾ 450 Kendall Street Cambridge, MA 02142	2,596,392	13.54%	2,596,392	10.05%
OrbiMed Private Investments V, LP ⁽⁴⁾ 601 Lexington Avenue, 54th Floor New York, NY 10022-4629	2,546,295	13.28%	2,546,295	9.85%
Pfizer Inc. ⁽⁵⁾ 235 East 42nd Street New York, NY 10017	1,387,639	7.24%	1,387,639	5.37%
667, L.P. and Baker Brothers Life Sciences, L.P. ⁽⁶⁾ 667 Madison Avenue, 21st Floor New York, NY 10065	1,164,020	6.07%	1,164,020	4.50%
Directors and Named Executive Officers:				
Keith M. Gottesdiener ⁽⁷⁾	676,434	3.51%	676,434	2.61%
Bart Henderson ⁽⁸⁾	308,690	1.60%	308,690	1.19%
Fred T. Fiedorek, M.D. ⁽⁹⁾	—	*	—	*%
Todd Foley	—	—	—	—%
Ed Mathers	—	—	—	—%
Neil Exter	—	—	—	—%
Christophe R. Jean	—	—	—	—%
Jonathan T. Silverstein, J.D.	—	—	—	—%
David Meeker ⁽¹⁰⁾	—	*	—	*%
David McGirr ⁽¹¹⁾	—	*	—	*%
All executive officers and directors as a group (13 persons) ⁽¹²⁾	1,459,019	7.58%	1,459,019	5.63%

* Represents beneficial ownership of less than 1%.

- (1) Consists of (i) 29,378 shares of common stock and (ii) 4,332,928 shares of common stock underlying shares of convertible preferred stock directly held by NEA Ventures 2009, L.P., or NEA 2009 New Enterprise Associates 13, L.P., or NEA 13. The shares held directly by NEA 2009 are indirectly held by Karen P. Welsh, the general partner of NEA 2009 and the shares held by NEA 13 are indirectly held by NEA Partners 13, L.P., or Partners 13, which is the sole general partner of NEA 13; NEA 13 GP, LTD, or NEA 13 LTD, which is the sole general partner of Partners 13; and each of the individual directors of NEA 13 LTD. The individual Directors of NEA 13 LTD, or the NEA 13

Directors, are M. James Barrett, Peter J. Barris, Forest Baskett, Patrick J. Kerins, David M. Mott, Scott D. Sandell and Ravi Viswanathan. Karen P. Welsh holds voting and dispositive power with regard to the shares held by NEA 2009. NEA Partners 13, NEA 13 LTD, and the NEA 13 Directors share voting and dispositive power with regard to the shares owned directly by NEA 13. All indirect holders of the above referenced shares disclaim beneficial ownership of all applicable shares except to the extent of their actual pecuniary interest therein.

- (2) Consists of (i) 17,627 shares of common stock and (ii) 3,963,810 shares of common stock underlying shares of convertible preferred stock held directly by Third Rock Ventures, L.P., or TRV LP. Each of Third Rock Ventures GP, LP, or TRV GP, the general partner of TRV LP, and Third Rock Ventures GP, LLC, TRV LLC, the general partner of TRV GP, and Mark Levin, Kevin Starr and Robert Tepper, the managers of TRV LLC, may be deemed to share voting and investment power over the shares held by TRV LP. Each of the reporting persons disclaims beneficial ownership of such shares, except to the extent of their proportionate pecuniary interest therein, if any.
- (3) Consists of (i) 29,378 shares of common stock and (ii) 2,567,014 shares of common stock underlying shares of convertible preferred stock held directly by MPM BioVentures V, L.P. and MPM Asset Management Investors BV5 LLC. MPM BioVentures V LLC is the Managing Member of MPM BioVentures V GP LLC, which is the General Partner of MPM BioVentures V, L.P. MPM BioVentures V LLC is the Manager of MPM Asset Management Investors BV5 LLC. Todd Foley, one of our directors, is a Member of MPM BioVentures V LLC and shares the power to vote, hold and dispose of the shares held by MPM BioVentures V, L.P., and MPM Asset Management Investors BV5 LLC. Mr. Foley and each such other Member of MPM BioVentures V LLC disclaims beneficial ownership of the securities reported herein except to the extent of his respective pecuniary interest therein.
- (4) Consists of shares of common stock underlying shares of convertible preferred stock held by OrbiMed Private Investments V, LP, or OPI V. OrbiMed Capital GP V LLC, or GP V, is the sole general partner of OPI V, and OrbiMed Advisors LLC, or Advisors, a registered adviser under the Investment Advisers Act of 1940, as amended, is the sole managing member of GP V. Samuel D. Isaly, or Isaly, a natural person, is the managing member of, and holder of a controlling interest in, Advisors. By virtue of such relationships, GP V, Advisors and Isaly may be deemed to have voting and investment power with respect to the shares of series A preferred stock held by OPI V noted above and as a result may be deemed to have beneficial ownership over such shares of series A preferred stock. Jonathan T. Silverstein, one of our directors, is a Member of Advisors. Each of GP V, Advisors, Mr. Isaly and Mr. Silverstein disclaims beneficial ownership of the shares held by OPI V, except to the extent of its or his pecuniary interest therein if any.
- (5) Consists of shares of common stock underlying shares of convertible preferred stock held by Pfizer Inc. As of August 15, 2017, the board of directors of Pfizer Inc. is comprised of the following individuals: Dennis A. Ausiello, Ronald E. Blaylock, W. Don Cornwell, Joseph J. Echevarria, Frances D. Fergusson, Helen H. Hobbs, James M. Kilts, Shantanu Narayen, Suzanne Nora Johnson, Ian C. Read, Stephen W. Sanger and James C. Smith. Pfizer Inc. is a publicly-traded company.
- (6) Consists of shares of common stock underlying shares of series A preferred stock held by 667, L.P., or 667 LP, and Baker Brothers Life Sciences, L.P., or Baker Brothers Life Sciences. Baker Bros. Advisors LP, or Baker Bros. Advisors, is the investment adviser to 667 LP and Baker Brothers Life Sciences and, pursuant to amended and restated management agreements between Baker Bros. Advisors, 667 LP and Baker Brothers Life Sciences and the respective general partners of 667 LP and Baker Brother Life Sciences, Baker Bros. Advisors has complete and unlimited discretion and authority with respect to the investments and voting power over investments of 667 LP and Baker Brothers Life Sciences. Baker Bros. Advisors disclaims beneficial ownership of all shares of series A

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preferred stock held by 667 LP and Baker Brothers Life Sciences except to the extent of any pecuniary interest therein.

- (7) Consists of (i) 558,277 shares of common stock, (ii) 27,262 shares of common stock underlying shares of series A preferred stock, and (iii) includes 90,895 shares of common stock underlying options that are exercisable within 60 days of September 22, 2017.
- (8) Consists of (i) 196,838 shares of common stock, (ii) 21,810 shares of common stock underlying shares of series A preferred stock, and (iii) includes 90,042 shares of common stock underlying options that are exercisable within 60 days of September 22, 2017.
- (9) Consists of (i) 104,420 shares of common stock, and (ii) includes 54,783 shares of common stock underlying options that are exercisable within 60 days of September 22, 2017.
- (10) Consists of (i) 21,810 shares of common stock, and (ii) 54,525 shares of common stock underlying shares of series A preferred stock (iii) includes 21,810 shares of common stock underlying options that are exercisable within 60 days of September 22, 2017.
- (11) Includes 43,620 shares of common stock underlying options that are exercisable within 60 days of September 22, 2017.
- (12) Consists of (i) 945,684 shares of common stock, (ii) 103,597 shares of common stock underlying shares of series A preferred stock, and (iii) includes 409,738 shares of common stock underlying options that are exercisable within 60 days of September 22, 2017.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock and provisions of our amended and restated certificate of incorporation and amended and restated bylaws as they will be in effect upon the consummation of this offering are summaries and are qualified in their entirety by reference to our amended and restated certificate of incorporation and amended and restated bylaws that will be in effect upon the closing of this offering, the forms of which are filed as exhibits to the registration statement of which this prospectus forms a part, and by applicable law.

Immediately prior to the consummation of this offering, we will file our amended and restated certificate of incorporation that authorizes 120,000,000 shares of common stock, \$0.001 par value per share, and 10,000,000 shares of preferred stock, \$0.001 par value per share. As of September 22, 2017, there were outstanding:

- 19,176,640 shares of our common stock, on an as-converted basis, held by approximately 30 stockholders of record; and
- 1,821,580 shares of our common stock issuable upon exercise of outstanding stock options.

In connection with this offering, we will effect a 1-for-9.17 reverse stock split of our outstanding common stock.

In August 2015, we effected a 93,500-for-1 forward stock split of our then-outstanding common stock. Also in August 2015, December 2015, January 2017 and August 2017, we sold 25,000,000 shares, 15,000,000 shares, 20,475,001 shares and 20,474,998 shares, respectively, of our series A preferred stock to certain investors. Following the stock split and the closing of our series A preferred stock financings, the LLC entity remained our largest stockholder, with the balance of our stock being owned by our series A investors. In August 2017, the LLC entity exchanged 8,578,646 of its shares of our common stock for 78,666,209 of newly-issued shares of our series A-1 junior preferred stock and the LLC entity distributed all of its shares of our series A-1 junior preferred stock to the holders of its preferred units and the remaining 1,617,646 shares of our common stock to the holders of its common units. We refer to the exchange and distribution as the Distribution. The series A-1 junior preferred stock will convert into shares of our common stock on a 9.17-for-one basis upon the closing of this offering. See "Corporate Reorganization."

Upon consummation of this offering, our authorized capital stock will consist of 120,000,000 shares of common stock, par value \$0.001 per share and 10,000,000 shares of preferred stock, par value \$0.001 per share. Unless our board of directors determines otherwise, we will issue all shares of our capital stock in uncertificated form. Assuming (1) the conversion of all outstanding shares of our preferred stock into 17,406,338 shares of our common stock and (2) the issuance by us of 6,666,666 shares of common stock in this offering, there will be 25,843,306 shares of common stock and no shares of preferred stock outstanding upon closing of this offering.

Common Stock

Holders of shares of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of stockholders. The holders of a plurality of the shares of our common stock entitled to vote in any election of directors can elect all of the directors standing for election.

Holders of shares of our common stock are entitled to receive dividends when and if declared by our board of directors out of funds legally available therefor, subject to any statutory or contractual restrictions on the payment of dividends and to any restrictions on the payment of dividends imposed by the terms of any outstanding preferred stock.

Upon our dissolution or liquidation or the sale of all or substantially all of our assets, after payment in full of all amounts required to be paid to creditors and to the holders of preferred stock having liquidation

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preferences, if any, the holders of shares of our common stock will be entitled to receive pro rata our remaining assets available for distribution.

Holders of shares of our common stock do not have preemptive, subscription, redemption or conversion rights.

Preferred Stock

Upon consummation of this offering, each share of our preferred stock will be converted into shares of our common stock on a 9.17-for-1 basis.

Our amended and restated certificate of incorporation authorizes our board of directors to establish one or more series of preferred stock (including convertible preferred stock). Unless required by law or by any stock exchange, the authorized shares of preferred stock will be available for issuance without further action by our stockholders. Our board of directors is able to determine, with respect to any series of preferred stock, the terms and rights of that series, including:

- the designation of the series;
- the number of shares of the series, which our board may, except where otherwise provided in the preferred stock designation, increase or decrease, but not below the number of shares then outstanding;
- the voting rights, if any, of the holders of the series;
- whether dividends, if any, will be cumulative or non-cumulative and the dividend rate of the series;
- the dates at which dividends, if any, will be payable;
- the rights of priority and amounts payable, if any, on shares of the series in the event of any voluntary or involuntary liquidation, dissolution or winding-up of the affairs of our company;
- the redemption rights and price or prices, if any, for shares of the series;
- the terms of any purchase, retirement or sinking fund, if any, provided for shares of the series;
- the terms, if any, upon which the shares of the series will be convertible into or exchangeable for shares of any other class, classes or series or other securities, whether or not issued by our company or any other entity;
- restrictions, if any, upon issuance of indebtedness of our company so long as any shares of the series are outstanding; and
- restrictions, if any, on the issuance of shares of the same series or of any other class or series.

We could issue a series of preferred stock that could, depending on the terms of the series, impede or discourage an acquisition attempt or other transaction that some, or a majority, of our stockholders might believe to be in their best interests or in which our stockholders might receive a premium for their shares of common stock over the market price of the shares of common stock.

Options

Upon completion of the offering, we will have 1,821,580 options to purchase our common stock outstanding. See "Executive and Director Compensation—Employee Benefit and Stock Plans" for a discussion of the terms of the Plan.

Authorized but Unissued Capital Stock

The Delaware General Corporation Law does not require stockholder approval for any issuance of authorized shares. However, the listing requirements of NASDAQ, which would apply so long as our common stock remains listed on NASDAQ, require stockholder approval of certain issuances equal to or exceeding 20% of the then outstanding voting power or then outstanding number of shares of common stock. These additional shares may be used for a variety of corporate purposes, including future public offerings, to raise additional capital or to facilitate acquisitions.

One of the effects of the existence of unissued and unreserved common stock or preferred stock may be to enable our board of directors to issue shares to persons friendly to current management, which issuance could render more difficult or discourage an attempt to obtain control of our company by means of a merger, tender offer, proxy contest or otherwise, and thereby protect the continuity of our management and possibly deprive our stockholders of opportunities to sell their shares of common stock at prices higher than prevailing market prices.

Anti-Takeover Effects of Provisions of Delaware Law and Our Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws

Undesignated Preferred Stock

The ability to authorize undesignated preferred stock will make it possible for our board of directors to issue preferred stock with super voting, special approval, dividend or other rights or preferences on a discriminatory basis that could impede the success of any attempt to acquire us or otherwise effect a change in control of us. These and other provisions may have the effect of deferring, delaying or discouraging hostile takeovers, or changes in control or management of our company.

Requirements for Advance Notification of Stockholder Meetings, Nominations and Proposals

Our amended and restated certificate of incorporation provides that special meetings of the stockholders may be called only by or at the direction of our board of directors. Our amended and restated bylaws prohibit the conduct of any business at a special meeting other than as specified in the notice for such meeting. These provisions may have the effect of deferring, delaying or discouraging hostile takeovers, or changes in control or management of our company.

Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors. In order for any matter to be "properly brought" before a meeting, a stockholder will have to comply with advance notice requirements and provide us with certain information. Additionally, vacancies and newly created directorships may be filled only by a vote of a majority of the directors then in office, even though less than a quorum, and not by the stockholders. Our amended and restated bylaws allow the presiding officer at a meeting of the stockholders to adopt rules and regulations for the conduct of meetings which may have the effect of precluding the conduct of certain business at a meeting if the rules and regulations are not followed. These provisions may also defer, delay or discourage a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.

Our amended and restated certificate of incorporation provides that the board of directors is expressly authorized to adopt, amend or repeal our amended and restated bylaws.

No Cumulative Voting

The Delaware General Corporation Law provides that stockholders are not entitled to cumulate votes in the election of directors unless our amended and restated certificate of incorporation provides

otherwise. Our amended and restated certificate of incorporation does not expressly provide for cumulative voting.

Removal of Directors

In accordance with the terms of our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing of this offering, our board of directors will be divided into three staggered classes of directors of the same or nearly the same number and each will be assigned to one of the three classes. At each annual meeting of the stockholders, a class of directors will be elected for a three-year term to succeed the directors of the same class whose terms are then expiring. The initial term of office of the directors of Class I shall expire as of the first annual meeting of our stockholders following the closing of this offering; the initial term of office of the directors of Class II shall expire as of the second annual meeting of our stockholders following the closing of this offering; and the initial term of office of the directors of Class III shall expire as of the third annual meeting of our stockholders following the closing of this offering.

- Our Class I directors will be Keith Gottesdiener and Christophe Jean;
- Our Class II directors will be Ed Mathers, Todd Foley, and Neil Exter; and
- Our Class III directors will be David Meeker and David McGirr.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the number of our directors shall be fixed from time to time by a resolution of the majority of our board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class shall consist of one third of the board of directors.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent stockholder efforts to effect a change of our management or a change in control.

Our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing of this offering also provide that our directors may be removed only for cause by the affirmative vote of the holders of at least 75% of the outstanding shares of capital stock entitled to vote in the election of directors or class of directors, voting together as a single class, at a meeting of the stockholders called for that purpose. This requirement of a supermajority vote to remove directors could enable a minority of our stockholders to prevent a change in the composition of our board. Any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by the vote of a majority of the remaining directors then in office, although less than a quorum, or by the sole remaining director.

Amendments to Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws

The Delaware General Corporation Law provides that, unless a corporation's certificate of incorporation provides otherwise, the affirmative vote of holders of shares constituting a majority of the votes of all shares entitled to vote may approve amendments to the certificate of incorporation.

Our amended and restated certificate of incorporation and amended and restated bylaws will provide that the affirmative vote of holders of at least 75% of the outstanding shares of capital stock, voting together as a single class, and entitled to vote in the election of directors will be required to amend, alter, change or repeal the amended and restated certificate of incorporation and the amended and restated bylaws. This requirement of a supermajority vote to approve amendments to our amended and restated certificate of incorporation and amended and restated bylaws could enable a minority of our stockholders to exercise veto power over such amendments.

Stockholder Action by Written Consent

Pursuant to Section 228 of the Delaware General Corporation Law, any action required to be taken at any annual or special meeting of the stockholders may be taken without a meeting, without prior notice and without a vote if a consent or consents in writing, setting forth the action so taken, is signed by the holders of outstanding stock having not less than the minimum number of votes that would be necessary to authorize or take such action at a meeting at which all shares of our stock entitled to vote thereon were present and voted, unless the corporation's certificate of incorporation provides otherwise. Our amended and restated certificate of incorporation will prohibit the taking of any action of our stockholders by written consent without a meeting.

Delaware Anti-Takeover Statute

We have not opted out of, and therefore are subject to, Section 203 of the Delaware General Corporation Law. Section 203 provides that, subject to certain exceptions specified in the law, a publicly-held Delaware corporation shall not engage in certain "business combinations" with any "interested stockholder" for a three-year period after the date of the transaction in which the person became an interested stockholder unless:

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding (1) shares owned by persons who are directors and also officers and (2) shares owned under employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- on or subsequent to the date of the transaction, the business combination is approved by the board and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least $66\frac{2}{3}\%$ of the outstanding voting stock which is not owned by the interested stockholder.

Generally, a business combination includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of a corporation's outstanding voting stock. Since Section 203 will apply to us, we expect that it would have an anti-takeover effect with respect to transactions our board of directors does not approve in advance. In such event, we would also anticipate that Section 203 could discourage attempts that might result in a premium over the market price for the shares of common stock held by stockholders.

Under certain circumstances, Section 203 makes it more difficult for a person who would be an "interested stockholder" to effect various business combinations with a corporation for a three-year period. The provisions of Section 203 may encourage companies interested in acquiring our company to negotiate in advance with our board of directors because the stockholder approval requirement would be avoided if our board of directors approves either the business combination or the transaction that results in the stockholder becoming an interested stockholder. These provisions also may make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Registration Rights

Following the closing of this offering, the holders of 18,858,976 shares of our common stock, or their transferees, will be entitled to the registration rights set forth below with respect to registration of the resale of such shares under the Securities Act pursuant to the investors' rights agreement, by and among us and certain of our stockholders.

Demand Registration Rights

At any time after 180 days after the effective date of this public offering as set forth on the cover page of this prospectus, upon the written request of at least a majority of the holders of the registrable securities then outstanding that we file a registration statement under the Securities Act covering the registration of registrable securities owned by such holder(s) having an anticipated aggregate offering price, net of selling expenses, of at least \$15.0 million, we will be obligated to notify all holders of registrable securities of such request. As soon as practicable thereafter, and in any event within 60 days after the date such request is received, we will be required to register the sale on a registration statement on Form S-1 of all registrable securities that holders may request to be registered, subject to specified exceptions, conditions and limitations. We may postpone the filing of a registration statement for up to 120 days once in any 12-month period if in the good faith judgment of our board of directors such registration would be materially detrimental to us, and we are not required to effect the filing of a registration statement during the period starting with the date that is 60 days prior to our good faith estimate of the date of filing of a registration statement initiated by us and ending on a date 180 days after the effective date of a registration statement initiated by us. The underwriters of any underwritten offering will have the right to limit the number of shares having registration rights to be included in the registration statement.

"Piggyback" Registration Rights

If we register any securities for public sale, holders of registration rights will have the right to include their shares in the registration statement. The underwriters of any underwritten offering will have the right to limit the number of registrable securities to be included in the registration statement, but such number may not be below 30% of the total number of shares included in such registration statement. The holders of registration rights have waived any and all rights to which they would otherwise be entitled to have their shares included in this offering.

Form S-3 Registration Rights

If we are eligible to file a registration statement on Form S-3, holders of at least 10% of our registrable securities then outstanding have the right to request that we file a registration statement on Form S-3, so long as the aggregate price to the public of the securities to be sold under the registration statement on Form S-3 is at least \$10.0 million or consists of all the remaining registrable securities, and subject to specified exceptions, conditions and limitations.

Expenses of Registration

Pursuant to the investors' rights agreement, we are generally required to bear all registration expenses, including the fees and expenses of one counsel, not to exceed \$50,000, representing the selling holders, incurred in connection with the demand, piggyback and Form S-3 registrations described above. We are not required to bear selling expenses, which include all underwriting discounts, selling commissions, stock transfer taxes applicable to the sale of registrable securities and fees and disbursements of any additional counsel for any selling holder. We are not required to pay registration expenses if the registration request under the investors' rights agreement is withdrawn at the request of the holders of a majority of the registrable securities unless (i) the holders of a majority of the registrable securities then

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outstanding agree to forfeit their right to one registration under the investors' rights agreement or (ii) the withdrawal is due to the discovery of a material adverse change in our business.

Termination of Registration Rights

The demand, piggyback and Form S-3 registration rights discussed above will terminate as to a given holder of registrable securities upon the earlier of (i) five years following the closing of this offering or (ii) such time as SEC Rule 144 or another similar exemption under the Securities Act is available for the sale of all shares held by the holder during a three-month period without registration and without the requirement for us to be in compliance with the current public information required under SEC Rule 144(c)(1).

Limitations of Liability and Indemnification

See "Executive and Director Compensation—Limitation on Liability and Indemnification Matters."

Market Listing

We have applied to list our common stock on the NASDAQ Global Market under the symbol "RYTM."

Transfer Agent and Registrar

Upon the completion of this offering, the transfer agent and registrar for our common stock will be Computershare.

MATERIAL UNITED STATES FEDERAL INCOME AND ESTATE TAX CONSEQUENCES TO NON-U.S. HOLDERS OF OUR COMMON STOCK

The following is a discussion of the material U.S. federal income and estate tax consequences of the acquisition, ownership, and disposition of our common stock to a non-U.S. holder that purchases shares of our common stock for cash in this offering. For purposes of this discussion, a "non-U.S. holder" means a beneficial owner (other than a partnership or other pass-through entity) of our common stock that is not, for U.S. federal income tax purposes:

- an individual who is a citizen or resident alien of the United States;
- a corporation or any other organization taxable as a corporation for U.S. federal income tax purposes, created or organized in the United States or under the laws of the United States or of any state thereof or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust if (i) the trust is subject to the primary supervision of a U.S. court and all substantial decisions of the trust are controlled by one or more U.S. persons or (ii) the trust has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

This discussion does not address the tax treatment of partnerships (or other entities that are treated as partnerships, grantor trusts, or other pass-through entities for U.S. federal income tax purposes) or persons that hold their common stock through partnerships, grantor trusts or such other pass-through entities. The tax treatment of a partner in a partnership or a holder of an interest in another pass-through entity that will hold our common stock generally will depend upon the status of the partner or interest holder and the activities of the partner or interest holder and the partnership or other pass-through entity, as applicable. Such a partner or interest holder should consult his, her, or its own tax advisor regarding the tax consequences of the acquisition, ownership and disposition of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based upon the provisions of the Code, the U.S. Treasury regulations promulgated thereunder, judicial decisions, and published rulings, administrative procedures and other guidance of the Internal Revenue Service, which we refer to as the IRS, all as in effect as of the date hereof. These authorities are subject to change and to differing interpretations, possibly with retroactive effect, which could result in U.S. federal income or estate tax consequences different from those summarized below. No ruling has been or will be sought from the IRS with respect to the matters summarized below, and there can be no assurance that the IRS will not take a contrary position regarding the U.S. federal income or estate tax consequences of the acquisition, ownership, or disposition of our common stock, or that any such contrary position would not be sustained by a court.

This discussion is not a complete analysis of all of the potential U.S. federal income and estate tax consequences relating to the acquisition, ownership, and disposition of our common stock by non-U.S. holders, nor does it address any U.S. federal gift tax or generation-skipping transfer tax consequences, any tax consequences arising under any state, local, or non-U.S. tax laws, the impact of any applicable tax treaty, any consequences under the Medicare contribution tax on net investment income, the alternative minimum tax, or any consequences under other U.S. federal tax laws. In addition, this discussion does not address tax consequences resulting from a non-U.S. holder's particular circumstances or to non-U.S. holders that may be subject to special tax rules, including, without limitation:

- non-U.S. governments, agencies or instrumentalities thereof, or entities they control;
- "controlled foreign corporations" and their shareholders;
- "passive foreign investment companies" and their shareholders;
- partnerships, grantor trusts or other entities that are treated as pass-through entities for U.S. federal income tax purposes, and their owners;

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- corporations that accumulate earnings to avoid U.S. federal income tax;
- former citizens or former long-term residents of the United States;
- banks, insurance companies or other financial institutions;
- tax-exempt pension funds or other tax-exempt organizations;
- persons who acquired our common stock pursuant to the exercise of employee stock options or otherwise as compensation;
- tax-qualified retirement plans;
- traders, brokers or dealers in securities, commodities or currencies;
- persons who hold our common stock as a position in a hedging transaction, wash sale, "straddle," "conversion transaction" or other risk reduction transaction or synthetic security;
- persons who do not hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, for investment purposes);
- persons who own or have owned, or are deemed to own or to have owned, more than 5% of our common stock (except to the extent specifically set forth below); or
- persons deemed to sell our common stock under the constructive sale provisions of the Code.

Prospective investors should consult their tax advisors regarding the particular U.S. federal income, estate, gift, and generation-skipping transfer tax consequences to them of acquiring, owning and disposing of our common stock, as well as any tax consequences arising under any state, local or foreign tax laws and any other U.S. federal tax laws. Prospective investors should also consult their tax advisors regarding the potential impact of any applicable income or estate tax treaty between the United States and such prospective investor's country of residence and of the rules described below under the heading "Foreign Account Tax Compliance Act."

Distributions on Common Stock

As described in the section entitled "Dividend Policy," we currently intend to retain all available funds and any future earnings for use in the operation of our business and do not anticipate paying any dividends on our common stock in the foreseeable future. The disclosure in this section addresses the consequences should our board of directors, in the future, determine to make a distribution of cash or property with respect to our common stock (other than certain distributions of stock which may be made free of tax), or to effect a redemption that is treated for tax purposes as a distribution. Any such distribution will generally constitute a dividend for U.S. federal tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent such a distribution exceeds both our current and our accumulated earnings and profits, such excess will be allocated ratably among the shares of common stock with respect to which the distribution is made, will constitute a return of capital, and will first be applied against and reduce the non-U.S. holder's adjusted tax basis in those shares of common stock, but not below zero. Distributions in excess of our current and accumulated earnings and profits and in excess of a non-U.S. holder's tax basis in that non-U.S. holder's shares of common stock then will be treated as gain from the sale of that common stock, subject to the tax treatment described below under "Gain on Disposition of Common Stock." A non-U.S. holder's adjusted tax basis in a share of common stock is generally the purchase price of the share, reduced by the amount of any distributions constituting a return of capital with respect to that share.

Any dividend paid to a non-U.S. holder of our common stock generally will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividend, or such lower rate as may be specified by an applicable income tax treaty between the United States and such non-U.S. holder's country of residence. If a non-U.S. holder is eligible for benefits under an income tax treaty and wishes to claim a reduced rate of withholding, the non-U.S. holder generally will be required to provide us or our paying

agent with a properly completed IRS Form W-8BEN, Form W-8BEN-E, or other applicable form, certifying under penalties of perjury the non-U.S. holder's qualification for the reduced rate. This certification must be provided to us or our paying agent prior to the payment of the dividend and may be required to be updated periodically. Special certification requirements apply to non-U.S. holders that hold common stock through certain foreign intermediaries. Non-U.S. holders that do not timely provide the required certifications, but that qualify for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. If we are not able to determine whether or not a distribution will exceed current and accumulated earnings and profits at the time the distribution is made, we may withhold tax on the entire amount of any distribution at the same rate as we would withhold on a dividend. However, a non-U.S. holder may obtain a refund of amounts that we withhold to the extent attributable to the portion of the distribution in excess of our current and accumulated earnings and profits.

If a non-U.S. holder holds our common stock in connection with the conduct of a trade or business in the U.S., and dividends paid on the common stock are effectively connected with the non-U.S. holder's U.S. trade or business (and, if required by an applicable income tax treaty between the United States and such non-U.S. holder's country of residence, are attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the U.S., as defined under the applicable treaty), the non-U.S. holder will be exempt from U.S. federal withholding tax on the dividends. To claim the exemption, the non-U.S. holder must furnish a properly executed IRS Form W-8ECI (or other applicable form) prior to the payment of the dividends. Any dividends paid on our common stock that are effectively connected with a non-U.S. holder's U.S. trade or business (and satisfy any other applicable treaty requirements) generally will be subject to U.S. federal income tax on a net income basis at the regular graduated U.S. federal income tax rates generally applicable to U.S. persons (as defined in the Code). A non-U.S. holder that is treated as a corporation for U.S. federal income tax purposes also may be subject to an additional branch profits tax equal to 30% (or such lower rate as is specified by an applicable income tax treaty between the United States and such non-U.S. holder's country of residence) of a portion of its earnings and profits for the taxable year that are effectively connected with a U.S. trade or business, as adjusted for certain items.

Gain on Disposition of Common Stock

Subject to the discussion below regarding backup withholding and foreign accounts, a non-U.S. holder generally will not be subject to U.S. federal income tax on any gain realized upon the sale, exchange, or other taxable disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a U.S. trade or business (and, if required by an applicable income tax treaty between the United States and such non-U.S. holder's country of residence, the gain is attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States), in which case the non-U.S. holder will generally be required to pay tax on the gain derived from the sale, exchange, or other taxable disposition (net of certain deductions or credits) under regular graduated U.S. federal income tax rates generally applicable to U.S. persons, and in the case of a non-U.S. holder that is treated as a corporation for U.S. federal income tax purposes, such non-U.S. holder may be subject to a branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such non-U.S. holder's country of residence;
- the non-U.S. holder is an individual who is present in the U.S. for a period or periods aggregating 183 days or more during the taxable year in which the sale, exchange, or other taxable disposition occurs and certain other conditions are met, in which case the non-U.S. holder will be subject to U.S. federal income tax at a flat 30% rate (or such lower rate as is specified by an applicable income tax treaty between the United States and such non-U.S. holder's country of residence) on the net gain derived from the sale, exchange, or other taxable disposition, which gain may be offset by U.S. source capital losses (even though the non-U.S. holder is not considered a resident of the United

States) provided that the non-U.S. holder has timely filed U.S. federal income tax returns reporting those losses; or

- our common stock is a "United States real property interest" by reason of our status as a "United States real property holding corporation," or USRPHC, for U.S. federal income tax purposes during the five-year period preceding such sale, exchange or other taxable disposition (or the non-U.S. holder's holding period, if shorter). Generally, a corporation is a USRPHC only if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business.

We believe we are not now and we do not anticipate becoming a USRPHC. However, there can be no assurance that we are not now a USRPHC or will not become one in the future. Even if we are or become a USRPHC, for so long as our common stock is "regularly traded," as defined by applicable U.S. Treasury regulations, on an established securities market, sales of our common stock generally will not be subject to tax for non-U.S. holders that have not held more than 5% of our common stock, actually or constructively, during the five-year period preceding such non-U.S. holder's sale, exchange or other taxable disposition of our common stock (or the non-U.S. holder's holding period, if shorter). If we are determined to be a USRPHC and the foregoing exception does not apply, then a purchaser may withhold 15% of the proceeds payable to a non-U.S. holder from a sale of our common stock and the non-U.S. holder generally will be taxed on its net gain derived from the disposition at the graduated U.S. federal income tax rates applicable to U.S. persons.

U.S. Federal Estate Tax

Shares of our common stock that are owned or treated as owned at the time of death by an individual who is not a citizen or resident of the United States, as specifically defined for U.S. federal estate tax purposes, are considered U.S. situs assets and will be included in the individual's gross estate for U.S. federal estate tax purposes. Such shares, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty between the United States and such individual's country of residence provides otherwise.

Information Reporting and Backup Withholding

Generally, we or certain financial middlemen must report annually to the IRS and to each non-U.S. holder the gross amount of dividends and other distributions on our common stock paid to the non-U.S. holder and the amount of tax withheld, if any, with respect to those distributions. Pursuant to applicable income tax treaties or other agreements, the IRS may make these reports available to tax authorities in the non-U.S. holder's country of residence or incorporation.

A non-U.S. holder may be subject to backup withholding with respect to dividends paid on shares of our common stock, unless, generally, the non-U.S. holder certifies under penalties of perjury (usually on IRS Form W-8BEN or W-8BEN-E) that the non-U.S. holder is not a U.S. person or otherwise establishes an exemption. The backup withholding rate is currently 28%. Dividends that are paid to non-U.S. holders subject to the withholding of U.S. federal income tax, as described above under the heading "Distributions on Common Stock" generally will be exempt from U.S. backup withholding.

Additional rules relating to information reporting requirements and backup withholding with respect to payments of the proceeds from the disposition of shares of our common stock are as follows:

- If the proceeds are paid to or through the U.S. office of a broker, the proceeds generally will be subject to backup withholding and information reporting, unless the non-U.S. holder certifies under penalties of perjury (usually on IRS Form W-8BEN or W-8BEN-E) that the non-U.S. holder is not a U.S. person and satisfies certain other requirements or otherwise establishes an exemption.

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- If the proceeds are paid to or through a non-U.S. office of a broker that is not a U.S. person and is not a foreign person with certain specified U.S. connections, which we refer to below as a "U.S.-related person," information reporting and backup withholding generally will not apply.
- If the proceeds are paid to or through a non-U.S. office of a broker that is a U.S. person or a U.S.-related person, the proceeds generally will be subject to information reporting (but not to backup withholding), unless the non-U.S. holder certifies under penalties of perjury (usually on IRS Form W-8BEN or W-8BEN-E) that the non-U.S. holder is not a U.S. person. A "U.S.-related person" includes (i) an entity classified as a "controlled foreign corporation" for U.S. federal income tax purposes, (ii) a foreign person, 50% or more of whose gross income from certain periods is effectively connected with a U.S. trade or business, or (iii) a foreign partnership if at any time during its tax year (a) one or more of its partners are U.S. persons who, in the aggregate, hold more than 50% of the income or capital interests of the partnership or (b) the foreign partnership is engaged in a U.S. trade or business.

Backup withholding is not an additional tax. Any amounts withheld from a non-U.S. holder under the backup withholding rules may be allowed as a refund or a credit against the non-U.S. holder's U.S. federal income tax liability, if any, provided that the non-U.S. holder timely furnishes the required information to the IRS. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Foreign Account Tax Compliance Act

Sections 1471 to 1474 of the Code (commonly referred to as the Foreign Account Tax Compliance Act, or FATCA) generally impose withholding tax on certain types of payments made to "foreign financial institutions" (as defined in the Code) and other non-U.S. entities unless those institutions and entities meet additional certification, information reporting and other requirements. FATCA generally imposes a 30% withholding tax on dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a foreign financial institution unless the foreign financial institution enters into an agreement with the U.S. Treasury to, among other things, (i) undertake to identify accounts held by certain U.S. persons (including certain equity and debt holders of such institution) or by U.S.-owned foreign entities, (ii) annually report certain information about such accounts, and (iii) withhold 30% on payments to account holders whose actions prevent it from complying with these reporting and other requirements. In addition, subject to certain exceptions, the legislation imposes a 30% withholding tax on the same types of payments to a "non-financial foreign entity" (as defined in the Code) unless the entity certifies that it does not have any substantial U.S. owners (which generally include any U.S. persons who directly or indirectly own more than 10% of the entity) or furnishes identifying information regarding each such substantial U.S. owner or agrees to report that information to the IRS. These withholding taxes will be imposed on dividends paid on our common stock, and, after December 31, 2018, on gross proceeds from sales or other dispositions of our common stock. Withholding under FATCA generally will not be reduced or limited by bilateral income tax treaties. However, intergovernmental agreements between the U.S. and other countries with respect to the implementation of FATCA and non-U.S. laws, regulations and other authorities enacted or issued with respect to those intergovernmental agreements may modify the FATCA requirements described above. Non-U.S. holders should consult their own tax advisors regarding the possible implications of FATCA on their investment in our common stock and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for shares of our common stock. We cannot predict the effect, if any, that future sales of shares of common stock, or the availability for future sales of shares of common stock, will have on the market price of shares of our common stock prevailing from time to time. The sale of substantial amounts of shares of our common stock in the public market, or the perception that such sales could occur, could harm the prevailing market price of shares of our common stock.

Currently 1,770,302 shares of our common stock are outstanding. Upon the conversion of our preferred stock to common stock prior to the closing of this offering, 19,176,640 shares of our common stock will be outstanding, and there will be 30 holders of our common stock.

Upon completion of this offering, we will have a total of 25,843,306 shares of our common stock outstanding (or 26,843,306 shares of common stock if the underwriters exercise in full their option to purchase additional shares of common stock). Of those shares, only the 6,666,666 shares sold in this offering will be freely tradable without restriction or further registration under the Securities Act by persons other than our "affiliates." Under the Securities Act, an "affiliate" of an issuer is a person who directly or indirectly controls, is controlled by or is under common control with that issuer. In addition, 4,018,538 shares of common stock may be granted under the 2017 Plan, which amount includes 1,821,580 shares subject to options currently outstanding.

Our amended and restated certificate of incorporation authorizes us to issue additional shares of common stock and options, rights, warrants and appreciation rights relating to common stock for the consideration and on the terms and conditions established by our board of directors in its sole discretion. In accordance with the Delaware General Corporation Law and the provisions of our amended and restated certificate of incorporation, we may also issue preferred stock that has designations, preferences, rights, powers and duties that are different from, and may be senior to, those applicable to shares of common stock. See "Description of Capital Stock."

Lock-Up Agreements

We, along with our directors, executive officers and all of our other stockholders have agreed with the underwriters that for a period of 180 days (the restricted period), after the date of this prospectus, subject to specified exceptions, we or they will not offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any shares of common stock or any securities convertible into or exercisable or exchangeable for shares of common stock, or enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common stock. All of our outstanding shares are subject to a lock-up agreement. Upon expiration of the "restricted" period, certain of our stockholders will have the right to require us to register their shares under the Securities Act. See "—Registration Rights" below and "Description of Capital Stock—Registration Rights."

After this offering, certain of our employees, including our executive officers and/or directors, may enter into written trading plans that are intended to comply with Rule 10b5-1 under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Sales under these trading plans would not be permitted until the expiration of the lock-up agreements relating to the offering described above.

Registration Rights

Upon closing of this offering, the holders of 18,858,976 shares of our common stock will be entitled to rights with respect to the registration of their shares under the Securities Act, subject to the lock-up agreements described under "—Lock-Up Agreements" above. Registration of these shares under the

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Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates, immediately upon the effectiveness of the registration statement of which this prospectus is a part. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock. See "Description of Capital Stock—Registration Rights."

Rule 144

In general, under Rule 144 a person (or persons whose shares are aggregated) who may be deemed our affiliate is entitled to sell within any three-month period a number of restricted securities that does not exceed the greater of 1% of the then outstanding shares of common stock and the average weekly trading volume during the four calendar weeks preceding each such sale, provided that at least six months has elapsed since such shares of common stock were acquired from us or any affiliate of ours and certain manner of sale, notice requirements and requirements as to availability of current public information about us are satisfied. Any person who is deemed to be our affiliate must also comply with such provisions of Rule 144 (other than the six-month holding period requirement) in order to sell shares of common stock which are not restricted securities (such as shares of common stock acquired by affiliates through purchases in the open market following this offering). Upon completion of this offering, 19,176,640 shares of our common stock will be "restricted securities" as such term is defined in Rule 144. A person who is not our affiliate, and who has not been our affiliate at any time during the 90 days preceding any sale, is entitled to sell shares of common stock (i) subject only to the requirements as to availability of current public information about us, provided that a period of at least six months has elapsed since the shares of common stock were acquired from us or any affiliate of ours, and (ii) without regard to the requirements as to availability of current public information about us or any other requirement of Rule 144, provided that at least one year has elapsed since the shares of common stock were acquired from us or any affiliate of ours.

Stock Options

As soon as practicable after the completion of this offering, we intend to file a Form S-8 registration statement under the Securities Act to register shares of our common stock subject to options outstanding or reserved for issuance under the 2017 Plan. This registration statement will become effective immediately upon filing, and shares covered by this registration statement will thereupon be eligible for sale in the public markets, subject to vesting restrictions, the lock-up agreements described above and Rule 144 limitations applicable to affiliates. For a more complete discussion of our stock plans, see "Executive and Director Compensation—Employee Benefit and Stock Plans."

UNDERWRITING

Under the terms and subject to the conditions in an underwriting agreement dated the date of this prospectus, the underwriters named below, for whom Morgan Stanley & Co. LLC, Merrill Lynch, Pierce, Fenner & Smith Incorporated and Cowen and Company, LLC are acting as representatives, have severally agreed to purchase, and we have agreed to sell to them, severally, the number of shares indicated below:

<u>Underwriter</u>	<u>Number of Shares</u>
Morgan Stanley & Co. LLC	
Merrill Lynch, Pierce, Fenner & Smith	
Incorporated	
Cowen and Company, LLC	
Needham & Company, LLC	
Total	

The underwriters and the representatives are collectively referred to as the "underwriters" and the "representatives," respectively. The underwriters are offering the shares of common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus are subject to the approval of certain legal matters by their counsel and to certain other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered by this prospectus if any such shares are taken. However, the underwriters are not required to take or pay for the shares covered by the underwriters' option to purchase additional shares described below.

The underwriters initially propose to offer part of the shares of common stock directly to the public at the offering price listed on the cover page of this prospectus and part to certain dealers. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the representatives.

Certain of our existing principal stockholders, directors and their affiliated entities, have indicated an interest in purchasing an aggregate of approximately \$40.0 million in shares of our common stock in this offering at the initial public offering price per share and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers, and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering. The underwriters will receive the same underwriting discount and commissions on these shares as they will on any other shares sold to the public in this offering.

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to 1,000,000 additional shares of common stock at the public offering price listed on the cover page of this prospectus, less underwriting discounts and commissions. To the extent the option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase about the same percentage of the additional shares of common stock as the number listed next to the underwriter's name in the preceding table bears to the total number of shares of common stock listed next to the names of all underwriters in the preceding table.

The following table shows the per share and total public offering price, underwriting discounts and commissions, and proceeds before expenses to us. These amounts are shown assuming both no exercise

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and full exercise of the underwriters' option to purchase up to an additional 1,000,000 shares of common stock.

	<u>Per Share</u>	<u>No Exercise</u>	<u>Total</u> <u>Full Exercise</u>
Public offering price	\$	\$	\$
Underwriting discounts and commissions to be paid by us	\$	\$	\$
Proceeds, before expenses, to us	\$	\$	\$

The estimated offering expenses payable by us, exclusive of the underwriting discounts and commissions, are approximately \$2.4 million. We have agreed to reimburse the underwriters for certain legal fees up to \$140,000 and expenses relating to clearance of this offering with the Financial Industry Regulatory Authority up to \$30,000.

The underwriters have informed us that they do not intend sales to discretionary accounts to exceed 5% of the total number of shares of common stock offered by them.

We intend to apply to have our common stock approved for quotation on the NASDAQ Global Market under the trading symbol "RYTM."

We and all directors and officers and the holders of substantially all of our outstanding stock and stock options have agreed that, without the prior written consent of Morgan Stanley & Co. LLC, Merrill Lynch, Pierce, Fenner & Smith Incorporated and Cowen and Company, LLC on behalf of the underwriters, we and they will not, during the period ending 180 days after the date of this prospectus, the restricted period:

- offer, sell, contract to sell, pledge or otherwise dispose of, (or enter into any transaction which is designed to, or might reasonably be expected to, result in the disposition (whether by actual disposition or effective economic disposition due to cash settlement or otherwise), directly or indirectly) any capital stock or any securities convertible into, or exercisable or exchangeable for such capital stock;
- file any registration statement with the SEC (other than a registration statement on Form S-8) relating to the offering of any shares of capital stock or any securities convertible into or exercisable or exchangeable for capital stock; or
- establish or increase a put equivalent position or liquidate or decrease a call equivalent position within the meaning of Section 16 of the Exchange Act and the rules and regulations of the SEC promulgated thereunder with respect to any shares of capital stock or any securities convertible into or exercisable or exchangeable for capital stock;

whether any such transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise. In addition, we and each such person agrees that, without the prior written consent of Morgan Stanley & Co. LLC, Merrill Lynch, Pierce, Fenner & Smith Incorporated and Cowen and Company, LLC on behalf of the underwriters, we or such other person will not, during the restricted period, make any demand for, or exercise any right with respect to, the registration of any shares of common stock or any security convertible into or exercisable or exchangeable for common stock.

The restrictions described in the immediately preceding paragraph do not apply to:

- the sale of shares to the underwriters; or
- the issuance by us of shares of common stock upon the exercise of an option or a warrant or the conversion of a security outstanding on the date of this prospectus of which the underwriters have been advised in writing;

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- transactions by any person other than us relating to shares of common stock or other securities acquired in open market transactions after the completion of the offering of the shares; provided that no filing under Section 16(a) of the Exchange Act is required or voluntarily made in connection with subsequent sales of the common stock or other securities acquired in such open market transactions; or
- the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock, provided that (i) such plan does not provide for the transfer of common stock during the restricted period and (ii) to the extent a public announcement or filing under the Exchange Act, if any, is required or voluntarily made regarding the establishment of such plan, such announcement or filing shall include a statement to the effect that no transfer of common stock may be made under such plan during the restricted period.

Morgan Stanley & Co. LLC, Merrill Lynch, Pierce, Fenner & Smith Incorporated and Cowen and Company, LLC, in their sole discretion, may release the common stock and other securities subject to the lock-up agreements described above in whole or in part at any time.

In order to facilitate the offering of the common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the option. The underwriters can close out a covered short sale by exercising the option or purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under the option. The underwriters may also sell shares in excess of the option, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering. As an additional means of facilitating this offering, the underwriters may bid for, and purchase, shares of common stock in the open market to stabilize the price of the common stock. These activities may raise or maintain the market price of the common stock above independent market levels or prevent or retard a decline in the market price of the common stock. The underwriters are not required to engage in these activities and may end any of these activities at any time.

We and the underwriters have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act.

A prospectus in electronic format may be made available on websites maintained by one or more underwriters, or selling group members, if any, participating in this offering. The representatives may agree to allocate a number of shares of common stock to underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters that may make Internet distributions on the same basis as other allocations.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their respective affiliates have, from time to time, performed, and may in the future perform, various financial advisory and investment banking services for us, for which they received or will receive customary fees and expenses.

In addition, in the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own

account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investment and securities activities may involve our securities and instruments. The underwriters and their respective affiliates may also make investment recommendations or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long or short positions in such securities and instruments.

Pricing of the Offering

Prior to this offering, there has been no public market for our common stock. The initial public offering price was determined by negotiations between us and the representatives. Among the factors considered in determining the initial public offering price were our future prospects and those of our industry in general, our sales, earnings and certain other financial and operating information in recent periods, and the price-earnings ratios, price-sales ratios, market prices of securities, and certain financial and operating information of companies engaged in activities similar to ours.

Selling Restrictions

European Economic Area

In relation to each Country of the European Economic Area which has implemented the Prospectus Directive, each, a Relevant Country, an offer to the public of any shares of our common stock may not be made in that Relevant Country, except that an offer to the public in that Relevant Country of any shares of our common stock may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Country:

(a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

(b) to fewer than 100 or, if the Relevant Country has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives for any such offer; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares of our common stock shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any shares of our common stock in any Relevant Country means the communication in any form and by any means of sufficient information on the terms of the offer and any shares of our common stock to be offered so as to enable an investor to decide to purchase any shares of our common stock, as the same may be varied in that Relevant Country by any measure implementing the Prospectus Directive in that Relevant Country, the expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Country), and includes any relevant implementing measure in the Relevant Relevant Country, and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

United Kingdom

Each underwriter has represented and agreed that:

(a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000, or FSMA, received by it in connection

with the issue or sale of the shares of our common stock in circumstances in which Section 21(1) of the FSMA does not apply to us; and

(b) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares of our common stock in, from or otherwise involving the United Kingdom.

Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Notice to Prospective Investors in Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company or the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA (FINMA), and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Notice to Prospective Investors in the Dubai International Financial Centre

This prospectus relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority, or DFSA. This prospectus is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus nor taken steps to verify the information

set forth herein and has no responsibility for the prospectus. The shares to which this prospectus relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares offered should conduct their own due diligence on the shares. If you do not understand the contents of this prospectus you should consult an authorized financial advisor.

Notice to Prospective Investors in Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of Non-CIS Securities may not be circulated or distributed, nor may the Non-CIS Securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or SFA, (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the Non-CIS Securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

(a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

(b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the Non-CIS Securities pursuant to an offer made under Section 275 of the SFA except:

(a) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

(b) where no consideration is or will be given for the transfer;

(c) where the transfer is by operation of law;

(d) as specified in Section 276(7) of the SFA; or

(e) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Notice to Prospective Investors in Hong Kong

The securities have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the securities has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or

only to "professional investors" as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Notice to Prospective Investors in Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) and, accordingly, will not be offered or sold, directly or indirectly, in Japan, or for the benefit of any Japanese Person or to others for re-offering or resale, directly or indirectly, in Japan or to any Japanese Person, except in compliance with all applicable laws, regulations and ministerial guidelines promulgated by relevant Japanese governmental or regulatory authorities in effect at the relevant time. For the purposes of this paragraph, "Japanese Person" shall mean any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

Notice to Prospective Investors in Australia

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission, in relation to the offering. This prospectus does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001, or Corporations Act, and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the shares may only be made to persons, or Exempt Investors, who are "sophisticated investors" (within the meaning of section 708(8) of the Corporations Act), "professional investors" (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the shares without disclosure to investors under Chapter 6D of the Corporations Act.

The shares applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring shares must observe such Australian on-sale restrictions.

This prospectus contains general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Morgan, Lewis & Bockius LLP, Boston, Massachusetts. Certain legal matters in connection with this offering will be passed upon for the underwriters by Wilmer Cutler Pickering Hale and Dorr LLP, New York, New York.

EXPERTS

The financial statements of Rhythm Pharmaceuticals, Inc. as of December 31, 2015 and 2016, and for the years then ended, included in this prospectus and the registration statement have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon (which contains an explanatory paragraph describing conditions that raise substantial doubt about the Company's ability to continue as a going concern as described in Note 1 to the financial statements) appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 (including exhibits, schedules, and amendments) under the Securities Act with respect to the shares of common stock offered by this prospectus. This prospectus does not contain all the information set forth in the registration statement. For further information about us and the shares of common stock to be sold in this offering, you should refer to the registration statement. Statements contained in this prospectus relating to the contents of any contract, agreement or other document are not necessarily complete and are qualified in all respects by the complete text of the applicable contract, agreement or other document, a copy of which has been filed as an exhibit to the registration statement. Whenever this prospectus refers to any contract, agreement, or other document, you should refer to the exhibits that are a part of the registration statement for a copy of the contract, agreement, or document.

You may read and copy all or any portion of the registration statement or any other information we file at the SEC's public reference room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can request copies of these documents, upon payment of a duplicating fee, by writing to the SEC. Please call the SEC at 1-800-SEC-0330 for further information about the operation of the public reference rooms. Our SEC filings, including the registration statement, are also available to you on the SEC's Website (<http://www.sec.gov>).

Upon completion of this offering, we will become subject to the information and periodic reporting requirements of the Exchange Act. Under the Exchange Act, we will file annual, quarterly and current reports, as well as proxy statements and other information with the SEC. These periodic reports, proxy statements, and other information will be available for inspection and copying at the SEC's Public Reference Room and the website of the SEC referred to above.

RHYTHM PHARMACEUTICALS, INC.
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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Shareholders of
Rhythm Pharmaceuticals, Inc.

We have audited the accompanying balance sheets of Rhythm Pharmaceuticals, Inc. as of December 31, 2015 and 2016, and the related statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the years then ended. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Rhythm Pharmaceuticals, Inc. at December 31, 2015 and 2016, and the results of its operations and its cash flows for the years then ended in conformity with U.S. generally accepted accounting principles.

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has recurring losses from operations and has a net capital deficiency that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to this matter are also described in Note 1. The financial statements do not include any adjustments that may result from the outcome of this uncertainty.

/s/ Ernst & Young LLP

Boston, Massachusetts
May 23, 2017

except for Note 13, as to which the date is September 22, 2017

RHYTHM PHARMACEUTICALS, INC.

BALANCE SHEETS

(in thousands, except share and per share data)

	December 31,	June 30,	Pro Forma	
	2015	2016	June 30, 2017	June 30, 2017 (unaudited)
Assets				
Current assets:				
Cash and cash equivalents	\$ 34,869	\$ 6,540	\$ 8,723	\$ 29,198
Short-term investments	—	3,997	9,017	9,017
Prepaid expenses and other current assets	623	638	722	722
Total current assets	35,492	11,175	18,462	38,937
Property, plant and equipment, net	17	930	822	822
Deferred issuance costs	1,481	9	895	895
Due from Rhythm Holding Company, LLC	60	—	—	—
Restricted cash	225	225	225	225
Total assets	\$ 37,275	\$ 12,339	\$ 20,404	\$ 40,879
Liabilities, convertible preferred stock and stockholders' equity (deficit)				
Current liabilities:				
Accounts payable	\$ 1,428	\$ 1,895	\$ 1,293	\$ 1,293
Deferred grant income	249	—	—	—
Due to related party	635	105	—	—
Deferred rent	—	76	80	80
Accrued expenses and other current liabilities	2,962	2,655	3,470	3,470
Total current liabilities	5,274	4,731	4,843	4,843
Long-term liabilities:				
Series A investor instrument	—	—	410	—
Deferred rent	—	311	270	270
Total liabilities	5,274	5,042	5,523	5,113
Commitments and contingencies (Note 9)				
Series A Convertible Preferred Stock, \$1.00 par value: 80,950,000 shares authorized; 40,000,000 shares issued and outstanding at December 31, 2015 and 2016, 60,475,001 shares issued and outstanding at June 30, 2017, no shares issued and outstanding at June 30, 2017 (pro forma) (aggregate liquidation preferences of \$44,129 and \$66,977 at December 31, 2016 and June 30, 2017, respectively)				
	40,000	40,000	60,147	—
Stockholders' equity (deficit):				
Common stock, \$0.001 par value: 21,341,330 shares authorized; 10,196,292 shares issued and outstanding December 31, 2015 and 2016 and June 30, 2017; 19,023,984 shares issued and outstanding at June 30, 2017 (pro forma)	10	10	10	19
Additional paid-in capital	42,662	43,830	44,429	125,452
Accumulated deficit	(50,671)	(76,543)	(89,705)	(89,705)
Total stockholders' equity (deficit)	(7,999)	(32,703)	(45,266)	35,766
Total liabilities, convertible preferred stock and stockholders' equity	\$ 37,275	\$ 12,339	\$ 20,404	\$ 40,879

The accompanying notes are an integral part of these financial statements

RHYTHM PHARMACEUTICALS, INC.

STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(in thousands, except share and per share data)

	Year Ended December 31 2015	Year Ended December 31, 2016	Six Months Ended June 30,	
			2016	2017
Operating expenses:				
Research and development	\$ 7,148	\$ 19,594	\$ 8,544	\$ 10,270
General and administrative	3,425	6,311	2,585	2,873
Total operating expenses	10,573	25,905	11,129	13,143
Loss from operations	(10,573)	(25,905)	(11,129)	(13,143)
Other income (expense):				
Revaluation of Series A Investor Right/Obligation and Series A Investor Instrument	(500)	—	—	(82)
Interest income, net	—	33	14	63
Total other income (expense):	(500)	33	14	(19)
Net loss and comprehensive loss	\$ (11,073)	\$ (25,872)	\$ (11,115)	\$ (13,162)
Net loss attributable to common stockholders	\$ (12,000)	\$ (29,074)	\$ (12,711)	\$ (15,534)
Net loss attributable to common stockholders per common share, basic and diluted (Note 2)	\$ (1.18)	\$ (2.85)	\$ (1.25)	\$ (1.52)
Weighted average common shares outstanding, basic and diluted	10,196,292	10,196,292	10,196,292	10,196,292
Pro forma net loss attributable to common stockholders per common share, basic and diluted (unaudited)		\$ (1.78)		\$ (0.79)
Pro forma weighted average common shares outstanding, basic and diluted (unaudited)		14,558,342		16,729,487

The accompanying notes are an integral part of these financial statements

RHYTHM PHARMACEUTICALS, INC.

**STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND
STOCKHOLDERS' EQUITY (DEFICIT)**

(in thousands, except share and per share data)

	Series A Convertible Preferred Stock		Common Stock		Series A-1 Junior Preferred Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount			
			\$	10					
Balance at December 31, 2014	—	—	10,196,292	\$ 10	—	—	39,230	(39,598)	(358)
Equity contribution	—	—	—	—	—	—	2,094	—	2,094
Modification of warrant in connection with a license agreement	—	—	—	—	—	—	923	—	923
Stock compensation expense	—	—	—	—	—	—	298	—	298
Dividend to Rhythm Holding Company LLC (associated with common stock options granted to employees of Motus Therapeutics, Inc.)	—	—	—	—	—	—	2,695	—	2,695
Dividend to Rhythm Holding Company LLC (associated with common stock options granted to employees of Motus Therapeutics, Inc.)	—	—	—	—	—	—	(2,695)	—	(2,695)
Reclassification of Series A Investor Right/Obligation liability upon Series A second tranche closing	—	883	—	—	—	—	117	—	117
Issuance of Series A Convertible Preferred Stock	40,000,000	39,117	—	—	—	—	—	—	—
Net loss	—	—	—	—	—	—	(11,073)	(11,073)	(11,073)
Balance at December 31, 2015	40,000,000	40,000	10,196,292	\$ 10	—	—	42,662	(50,671)	(7,999)
Stock compensation expense	—	—	—	—	—	—	1,168	—	1,168
Net loss	—	—	—	—	—	—	(25,872)	(25,872)	(25,872)
Balance at December 31, 2016	40,000,000	40,000	10,196,292	\$ 10	—	—	43,830	(76,543)	(32,703)
Stock compensation expense	—	—	—	—	—	—	698	—	698
Change in unrealized loss on marketable securities	—	—	—	—	—	—	(1)	—	(1)
Net loss	—	—	—	—	—	—	(13,162)	(13,162)	(13,162)
Issuance of Series A Convertible Preferred Stock	20,475,001	20,147	—	—	—	—	(98)	—	(98)
Balance at June 30, 2017 (unaudited)	60,475,001	60,147	10,196,292	\$ 10	—	—	44,429	(89,705)	(45,266)
Settlement of Series A investor instrument	—	410	—	—	—	—	—	—	—
Issuance of Series A Convertible Preferred Stock	20,474,998	20,475	—	—	—	—	—	—	—
Exchange of common stock held by LLC entity for Series A-1 Junior Preferred Stock (Note 12)	—	—	(8,578,646)	(8)	78,666,209	79	(71)	—	—
Conversion of Series A Convertible Preferred Stock and Series A-1 Junior Preferred Stock into common stock on 9.17 to 1 basis	(80,949,999)	(81,032)	17,406,338	17	(78,666,209)	(79)	81,094	—	81,032
Pro-forma balance at June 30, 2017 (unaudited)	—	—	19,023,984	\$ 19	—	—	125,452	(89,705)	35,766

The accompanying notes are an integral part of these financial statements

RHYTHM PHARMACEUTICALS, INC.

STATEMENTS OF CASH FLOWS

(in thousands, except share and per share data)

	Year Ended December 31, 2015	Year Ended December 31, 2016	Six Months Ended June 30, 2016	Six Months Ended June 30, 2017
Operating activities				(unaudited)
Net loss	\$ (11,073)	\$ (25,872)	\$ (11,115)	\$ (13,162)
Adjustments to reconcile net loss to cash used in operating activities:				
Stock-based compensation expense	298	1,168	559	698
Depreciation and amortization	—	144	33	108
Non-cash rent expense	—	11	47	(37)
Modification of warrant in connection with license agreement	923	—	—	—
Mark to market revaluation of Series A Investor Right/Obligation and Series A Investor Instrument	500	—	—	82
Changes in operating assets and liabilities:				
Prepaid expenses and other current assets	(581)	41	(957)	(68)
Deferred issuance costs	(1,481)	1,472	(344)	(886)
Tenant improvement allowance	—	376	376	—
Restricted cash	(225)	—	—	—
Accounts payable	893	467	882	(602)
Deferred grant income	249	(249)	(249)	—
Due to Motus Therapeutics, Inc.	635	(635)	(133)	—
Due (from) to Rhythm Holding Company, LLC	(60)	165	60	(105)
Accrued expenses and other current liabilities	2,945	(307)	(1,756)	814
Net cash used in operating activities	<u>(6,977)</u>	<u>(23,219)</u>	<u>(12,597)</u>	<u>(13,158)</u>
Investing activities				
Purchases of short-term investments	—	(15,222)	(7,080)	(13,021)
Maturities of short-term investments	—	11,169	1,780	7,985
Purchases of property, plant and equipment	(17)	(1,057)	(986)	—
Net cash used in investing activities	<u>(17)</u>	<u>(5,110)</u>	<u>(6,286)</u>	<u>(5,036)</u>
Financing activities				
Net proceeds from issuance of Series A Convertible Preferred Stock	39,617	—	—	20,377
Equity contribution	2,094	—	—	—
Net cash provided by financing activities	<u>41,711</u>	<u>—</u>	<u>—</u>	<u>20,377</u>
Net increase (decrease) in cash and cash equivalents	<u>34,717</u>	<u>(28,329)</u>	<u>(18,883)</u>	<u>2,183</u>
Cash and cash equivalents at beginning of period	152	34,869	34,869	6,540
Cash and cash equivalents at end of period	<u>\$ 34,869</u>	<u>\$ 6,540</u>	<u>\$ 15,986</u>	<u>\$ 8,723</u>

The accompanying notes are an integral part of these financial statements

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements**

**(including data applicable to unaudited periods)
(Information as of June 30, 2017 and for the
six months ended June 30, 2016 and 2017 is unaudited)**

(In thousands, except share and per share information)

1. Nature of Business

Rhythm Pharmaceuticals, Inc. (the "Company"), is a biopharmaceutical company focused on the development and commercialization of peptide therapeutics for the treatment of genetic deficiencies that result in life-threatening metabolic disorders. The Company's lead product candidate is setmelanotide (RM-493), which is a potent, first-in-class, melanocortin-4, or MC4, receptor agonist for the treatment of rare genetic disorders of obesity caused by MC4 pathway deficiencies. The Company is currently evaluating setmelanotide for the treatment of six genetic disorders of obesity: pro-opiomelanocortin, or POMC, leptin receptor, or LepR, Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous, and POMC epigenetic disorders.

Corporate Reorganization

The Company is a Delaware corporation organized in February 2013 under the name Rhythm Metabolic, Inc. Prior to the Company's organization and the Corporate Reorganization referred to below, the Company was part of Rhythm Pharmaceuticals, Inc. (the "Predecessor Company"), a Delaware corporation which was organized in November 2008 and which commenced active operations in 2010.

In March 2013, the Predecessor Company underwent a corporate reorganization, (the "Corporate Reorganization"), pursuant to which all of the outstanding equity securities of the Predecessor Company were exchanged for units of Rhythm Holding Company, LLC, a newly-organized limited liability company (the "LLC entity"). After the consummation of this exchange and as part of the Corporate Reorganization, the Predecessor Company contributed setmelanotide and the MC4R agonist program to the Company and distributed to the LLC entity all of the then issued and outstanding shares of the Company's stock. The result of the Corporate Reorganization was that the Company and the Predecessor Company became wholly-owned subsidiaries of the LLC entity and the two product candidates and related programs that were originally held by the Predecessor Company were separated, with relamorelin and the ghrelin agonist program being retained by the Predecessor Company and setmelanotide and the MC4R agonist program being held by the Company. The Predecessor Company, after consummation of the Corporate Reorganization, is referred to within these Notes to Financial Statements as the Relamorelin Company and/or Motus.

On October 13, 2015, the Relamorelin Company changed its name to Motus Therapeutics, Inc ("Motus") and the Company changed its name to Rhythm Pharmaceuticals, Inc. On December 15, 2016, Motus was sold to a large pharmaceutical company. On August 21, 2017, the LLC entity distributed to its members all of its shares of the Company (see Note 12 for further discussion).

Liquidity

The Company has incurred operating losses and negative cash flows from operations since inception, incurred a net loss of \$25,872 and \$13,162 during the year ended December 31, 2016 and the six months ended June 30, 2017, respectively, and has an accumulated deficit of \$89,705 as of June 30, 2017. The Company has primarily funded these losses through capital contributions received from the LLC entity and the sale of preferred stock to outside investors. To date, the Company has no product revenue and

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

**(including data applicable to unaudited periods)
(Information as of June 30, 2017 and for the
six months ended June 30, 2016 and 2017 is unaudited)**

(In thousands, except share and per share information)

1. Nature of Business (Continued)

management expects operating losses to continue for the foreseeable future. The Company has devoted substantially all of its resources to its drug development efforts, comprising research and development, manufacturing, conducting clinical trials for its product candidates, protecting its intellectual property and general and administrative functions relating to these operations. The future success of the Company is dependent on its ability to develop its product candidates and ultimately upon its ability to attain profitable operations. At June 30, 2017, the Company had \$17,740 of cash and cash equivalents and short-term investments on hand. In January 2017, the Company closed the first tranche on the sale of preferred stock resulting in net proceeds of \$20,377. The second tranche of \$20,475 closed in August 2017 (see Note 12 for further discussion).

The Company is subject to a number of risks, including the need for substantial additional capital for clinical research and product development. Based upon the Company's \$17,740 in existing cash, cash equivalents and short-term investments as of June 30, 2017, the Company does not have sufficient existing cash, cash equivalents and short-term investments to support operations for at least the next year following the date that the financial statements are issued.

The conditions in the preceding paragraph raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the financial statements are issued. Management's plans to alleviate the conditions that raise substantial doubt regarding the Company's ability to continue as a going concern include pursuing one or more of the following steps to raise additional funding and/or reduce expenditures:

- Raise funding through the possible sales of the Company's common or preferred stock, including public or private equity financings.
- Seek a partner to advance development of setmelanotide for the potential treatment of one or more genetic disorders of obesity.
- Defer or terminate planned clinical trials.

There can be no assurance, however, that the Company will receive cash proceeds from any of these potential resources or reduce its operating expenses. Furthermore, to the extent cash proceeds are received or expenses are reduced, there can be no assurance that those proceeds or reductions in expenses would be sufficient to support the Company's operations for at least the next year following the date that the financial statements are issued. Management has concluded that the likelihood that its plans to obtain sufficient funding from one or more of these sources will be successful or its plans to reduce its operating expenses, while reasonably possible, is less than probable. Accordingly, management has concluded that substantial doubt exists regarding the Company's ability to continue as a going concern.

If the Company is unable to raise capital when needed or on attractive terms, or if it is unable to procure partnership arrangements to advance its programs, or if it is unable to reduce its operating expenses, the Company would be forced to delay, reduce or eliminate its research and development programs and any future commercialization efforts.

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

**(including data applicable to unaudited periods)
(Information as of June 30, 2017 and for the
six months ended June 30, 2016 and 2017 is unaudited)**

(In thousands, except share and per share information)

1. Nature of Business (Continued)

The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the ordinary course of business. The financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of the uncertainties described above.

2. Summary of Significant Accounting Policies***Basis of Presentation***

The Company's financial statements have been prepared in conformity with accounting principles generally accepted in the United States ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

The Company has historically existed and functioned as part of the consolidated businesses of the Predecessor Company. As noted above, the Predecessor Company's setmelanotide and the MC4R agonist program were transferred to the Company as part of the Corporate Reorganization on March 21, 2013. These financial statements include the results of operations of setmelanotide and the MC4R agonist program from its inception. As part of the Corporate Reorganization, the Company also entered into a formal payroll services intercompany agreement with the Relamorelin Company. On November 16, 2016, the employees of the Relamorelin Company that were providing services to the Company, terminated their employment contracts with the Relamorelin Company and entered into new employment agreements with the Company. On December 15, 2016, the Relamorelin Company closed on its sale to a large pharmaceutical company. At June 30, 2017, the Company had ten employees directly employed by the Company. During 2015 and 2016, costs have been allocated to the Company for the purposes of preparing the financial statements based on a specific identification basis or, when specific identification is not practicable, a proportional cost allocation method which allocates expenses based upon the percentage of employee time and research and development effort expended on the Company's business as compared to total employee time and research and development effort of the combined Motus and Rhythm. The proportional use basis adopted to allocate shared costs is in accordance with the guidance of SEC Staff Accounting Bulletin ("SAB") Topic 1B, *Allocation Of Expenses And Related Disclosure In Financial Statements Of Subsidiaries, Divisions Or Lesser Business Components Of Another Entity*. Management has determined that the method of allocating costs to the Company is reasonable. Cost allocation was no longer required subsequent to the 2016 sale of the Relamorelin Company.

Management believes that the statements of operations include a reasonable allocation of costs and expenses incurred by the Relamorelin Company, which benefited the Company. However, such amounts may not be indicative of the actual level of costs and expenses that would have been incurred by the Company if it had operated as an independent company or of the costs and expenses expected to be incurred in the future. Management has not presented an estimate of what the expenses of the Company

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

**(including data applicable to unaudited periods)
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(In thousands, except share and per share information)

2. Summary of Significant Accounting Policies (Continued)

would have been on a standalone basis as it was not practicable to make a reasonable estimate. As such, the financial information herein may not necessarily reflect the financial position, results of operations and cash flows of the Company expected in the future or what it would have been had it been an independent company during the periods presented.

As described above, Relamorelin Company employee costs are allocated to the Company based on a proportional use method. For those employees who became employees of the Company on November 16, 2016, their full employment cost was \$3,155 and \$2,727 for the years ended December 31, 2015 and 2016, respectively.

On September 22, 2017, the Company's board of directors approved a 1-for-9.17 reverse stock split of the Company's issued and outstanding shares of common stock. All share and per share amounts in the financial statements and notes thereto have been retrospectively adjusted for all periods presented to give effect of the reverse stock split including reclassifying an amount equal to the reduction in par value of common stock to additional paid-in capital.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent liabilities at the date of the financial statements and the reported amounts of revenue and expenses during the reporting period. The Company bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes to be reasonable under the circumstances. This process may result in actual results differing materially from those estimated amounts used in the preparation of the financial statements if these results differ from historical experience, or other assumptions do not turn out to be substantially accurate, even if such assumptions are reasonable when made. Significant estimates relied upon in preparing these financial statements include the allocation of costs from the Relamorelin Company in accordance with SAB Topic 1B, accrued expenses, stock-based compensation expense, the valuation allowance on the Company's deferred tax assets, and the fair value of the Series A Investor Right/Obligations and the Series A Investor Call Options. See Note 4.

Unaudited Interim Presentation

The accompanying interim balance sheet as of June 30, 2017, the statements of operations and comprehensive loss and cash flows for the periods ended June 30, 2016 and 2017 and the statement of convertible preferred stock and stockholders' equity (deficit) for the six months ended June 30, 2017 and the related footnote disclosures are unaudited. These unaudited interim financial statements have been prepared in accordance with GAAP. In management's opinion, the unaudited interim financial statements have been prepared on the same basis as the audited financial statements and include all adjustments, which include only normal recurring adjustments necessary for the fair presentation of the interim financial statements. The results for the six months ended June 30, 2017 are not necessarily indicative of the results expected for the full fiscal year.

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

**(including data applicable to unaudited periods)
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(In thousands, except share and per share information)

2. Summary of Significant Accounting Policies (Continued)***Unaudited Pro Forma Financial Information***

The unaudited pro forma balance sheet and statement of convertible preferred stock and stockholders' equity (deficit) as of June 30, 2017 reflect the issuance of 20,474,998 shares of Series A Convertible Preferred Stock and the exchange of 8,578,646 shares of Common Stock for 78,666,209 shares of Series A-1 Junior Preferred Stock on August 21, 2017 and the conversion of all the outstanding shares of Series A Convertible Preferred Stock and Series A-1 Junior Preferred Stock into shares of Common Stock upon the closing of an initial public offering.

Unaudited pro forma net loss per share attributable to common stockholders for the year-ended December 31, 2015 and 2016 and the six months ended June 30, 2016 and 2017, is computed using the weighted-average number of common shares outstanding after giving effect to the conversion of all Preferred Stock into shares of the Common Stock as if such conversion had occurred at the beginning of the period presented, or the date of original issuance, if later. Accordingly, the pro forma basic and diluted net loss per share attributable to common stockholders does not include the effects of the cumulative Preferred Stock dividends.

Off-Balance Sheet Risk and Concentrations of Credit Risk

Financial instruments, which potentially subject the Company to significant concentration of credit risk, consist primarily of cash and cash equivalents and short-term investments, which are maintained at two federally insured financial institutions. The deposits held at these two institutions are in excess of federally insured limits. The Company has not experienced any losses in such accounts and management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held. The Company has no off-balance sheet risk, such as foreign exchange contracts, option contracts, or other foreign hedging arrangements.

Segment Information

Operating segments are defined as components of an entity about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment operating exclusively in the United States.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original or remaining maturity from the date of purchase of three months or less to be cash equivalents. Cash and cash equivalents includes bank demand deposits, U.S. treasury bills and money market funds that invest primarily in U.S. government treasuries.

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

**(including data applicable to unaudited periods)
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(In thousands, except share and per share information)

2. Summary of Significant Accounting Policies (Continued)***Short-term Investments***

Short-term investments consist of investments with original maturities greater than 90 days, as of the date of purchase. The Company has classified its investments with maturities beyond one year as short term, based on their highly liquid nature and because such marketable securities represent the investment of cash that is available for current operations. The Company considers its investment portfolio available-for-sale. Accordingly, these investments are recorded at fair value, which is based on quoted market prices. Unrealized gains and losses are reported as a component of accumulated other comprehensive income (loss) in stockholders' equity (deficit). Realized gains and losses and declines in value judged to be other than temporary are included as a component of other income (expense), net based on the specific identification method. When determining whether a decline in value is other than temporary, the Company considers various factors, including whether the Company has the intent to sell the security, and whether it is more likely than not that the Company will be required to sell the security prior to recovery of its amortized cost basis. Fair value is determined based on quoted market prices.

Restricted Cash

Restricted cash consists of a security deposit in the form of a letter of credit placed in a separate restricted bank account as required under the terms of the Company's new lease arrangement for its corporate office in Boston, Massachusetts.

Deferred Issuance Costs

Deferred issuance costs, which consist of direct incremental legal and accounting fees relating to the potential initial public offering ("IPO"), are capitalized. The deferred issuance costs will be offset against IPO proceeds upon the consummation of the offering. In the event the offering is terminated, deferred issuance costs will be expensed and included in non-current assets.

The Company had capitalized \$1,825 of deferred issuance costs related to prior registration statements confidentially submitted to the Securities and Exchange Commission in 2015 and 2016. In the fourth quarter of 2016, the Company wrote off these deferred issuance costs to general and administrative expenses because the offering was postponed significantly in excess of 90 days. As a result, the costs were not deemed realizable as the Company expects to incur similar costs in connection with its current planned IPO. The Company incurred \$9 and \$895 of deferred issuance costs as of December 31, 2016 and June 30, 2017, respectively, which is included in non-current assets.

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

**(including data applicable to unaudited periods)
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(In thousands, except share and per share information)

2. Summary of Significant Accounting Policies (Continued)***Prepaid Expenses and Other Current Assets***

Prepaid expenses and other current assets consist primarily of costs incurred in advance of services being received, including services related to clinical trial programs.

	December 31,		June 30,
	2015	2016	2017
Prepaid research and development costs	\$ 595	\$ 422	\$ 550
Other current assets	28	216	172
Prepaid expenses and other current assets	\$ 623	\$ 638	\$ 722

Property, Plant and Equipment

Property, Plant and Equipment consists of the following:

	Useful Life	December 31,		June 30,
		2015	2016	2017
Leasehold improvements	*	\$ 17	\$ 891	\$ 891
Office equipment	5 years	—	70	70
Computers and software	3 years	—	19	19
Furniture and fixtures	5 years	—	94	94
		17	1,074	1,074
Less accumulated depreciation and amortization		—	(144)	(252)
Property, Plant and Equipment, net		\$ 17	\$ 930	\$ 822

* Shorter of asset life or lease term.

Leasehold improvements made during the year ended December 31, 2015 represent costs related to the Company's newly-leased office space in Boston, Massachusetts. The assets were transferred into service in 2016 and are being amortized over the shorter of the lease term or their expected useful life.

2015 Series A Investor Right/Obligation, 2015 Series A Investor Call Option and 2017 Series A Investor Instrument

The Company classified its 2015 Series A Investor Right/Obligation, its 2015 Series A Investor Call Option and its 2017 Series A Investor Instrument (see Note 4) as liabilities as they are free-standing financial instruments. The 2015 Series A Investor Right/Obligation, the 2015 Series A Investor Call Option and 2017 Series A Investor Instrument were recorded at fair value upon the issuance of Series A Convertible Preferred Stock in August 2015 and January 2017, respectively, and subsequently remeasured to fair value. Changes in fair value of these financial instruments are recognized as a component of other income (expense), net in the Statement of Operations and Comprehensive Loss. The 2015 Series A

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

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2. Summary of Significant Accounting Policies (Continued)

Investor Right/Obligation was exercised and the 2015 Series A Investor Call Option expired on December 1, 2015 upon the 2015 Series A Second Tranche Closing.

The Company used the Black-Scholes option-pricing model, which incorporates assumptions and estimates, to value the 2015 and 2017 Series A Investor Call Options (see Note 4). The Company assessed these assumptions and estimates on a quarterly basis as additional information impacting the assumptions was obtained. Estimates and assumptions impacting the fair value measurement include the fair value per share of the underlying Series A Convertible Preferred Stock, the expected term of the Series A Investor Call Options, risk-free interest rate, expected dividend yield and expected volatility of the price of the underlying preferred stock. The Company determined the fair value per share of the underlying preferred stock by taking into consideration the most recent sale of its convertible preferred stock and the investors' right to invest in a subsequent tranche. The Company's history as a private company means that it lacks company-specific historical and implied volatility information of its stock. Therefore, it estimates its expected stock volatility based on the historical volatility of publicly traded peer companies for a term comparable to the estimated term of the Series A Investor Call Options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve for time periods approximately equal to the estimated term of the Series A Investor Call Options. A dividend yield of zero is assumed.

The Company estimated the fair value of the 2015 and 2017 Series A Investor Right/Obligations as the probability-weighted present value of the expected benefit of the investment (see Notes 4 and 5).

Government Grants

The Company obtained an Orphan Products Development grant entitled "Phase 2 study of the melanocortin 4 receptor agonist RM-493 for the treatment of Prader-Willi syndrome" in 36 patients. The grant was awarded by the Public Health Service ("PHS") Food and Drug Administration. The PHS grant is for a total of \$999 and is effective July 2015 through June 2018 for reimbursement of expenses relating to the Phase 2 Prader-Willi Study.

The Company recognizes government grants upon the determination that it will comply with the conditions attached to the grant arrangement and the grant will be received. Government grants are recognized in the statements of operations on a systematic basis over the periods in which the Company recognizes the related costs for which the government grant is intended to compensate. Government grants for research and development efforts are deducted in reporting the related expense in the statement of operations. Government grant income received during the year ended December 31, 2015 and 2016 and the six months ended June 30, 2016 and 2017 of \$147, \$642, \$249 and zero, respectively, is included as a deduction to research and development expense in the statements of operations. Deferred grant income on the balance sheet as of December 31, 2015 and 2016 and June 30, 2017 was \$249, zero and zero, respectively.

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

**(including data applicable to unaudited periods)
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(In thousands, except share and per share information)

2. Summary of Significant Accounting Policies (Continued)***Research and Development Expenses***

Costs incurred in the research and development of the Company's products are expensed to operations as incurred. Research and development expenses consist of costs incurred in performing research and development activities, including salaries and benefits, facilities costs, overhead costs, contract services and other outside costs, both directly incurred and allocated from the Relamorelin Company. The value of goods and services received from contract research organizations or contract manufacturing organizations in the reporting period are estimated based on the level of services performed and progress in the period for which the Company has not yet received an invoice from the supplier.

Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses, and expensed as the related goods are delivered or the services are performed.

Income Taxes

The Company is taxed as a C corporation for federal income tax purposes. Income taxes for the Company are recorded in accordance with FASB ASC Topic 740, *Income Taxes* ("ASC 740"), which provides for deferred taxes using an asset and liability approach. Income taxes have been calculated on a separate tax return basis. Certain of the Company's activities and costs have been included in the tax returns filed by the Relamorelin Company and the LLC entity. Prior to the Corporate Reorganization, the Company's operations were included in the tax returns filed by the Predecessor Company. The Company has filed tax returns on its own behalf since the Corporate Reorganization. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases using enacted tax rates in effect for the year in which the differences are expected to affect taxable income. Tax benefits are recognized when it is more likely than not that a tax position will be sustained during an audit. Deferred tax assets are reduced by a valuation allowance if current evidence indicates that it is considered more likely than not that these benefits will not be realized.

Net Loss Per Share Attributable to Common Shareholders

Basic net loss per share attributable to common stockholders is calculated by dividing net loss attributable to common stockholders by the weighted average shares outstanding during the period, without consideration for Common Stock equivalents. Net loss attributable to common stockholders is calculated by adjusting the net loss of the Company for cumulative preferred stock dividends. During periods of income, the Company allocates participating securities a proportional share of income determined by dividing total weighted average participating securities by the sum of the total weighted average common shares and participating securities (the "two class method"). The Company's convertible preferred stock participates in any dividends declared by the Company and are therefore considered to be participating securities. Participating securities have the effect of diluting both basic and diluted earnings per share during periods of income. During periods of loss, the Company allocates no loss to participating

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

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2. Summary of Significant Accounting Policies (Continued)

securities because they have no contractual obligation to share in the losses of the Company. Diluted net loss per share attributable to common stockholders is calculated by adjusting weighted average shares outstanding for the dilutive effect of Common Stock equivalents outstanding for the period, determined using the treasury-stock and if-converted methods. For purposes of the diluted net loss per share attributable to common stockholders calculation, convertible preferred stock and stock options are considered to be Common Stock equivalents but have been excluded from the calculation of diluted net loss per share attributable to common stockholders, as their effect would be anti-dilutive for all periods presented. Therefore, basic and diluted net loss per share were the same for all periods presented.

As the years ended December 31, 2015 and 2016 and the six months ended June 30, 2016 and 2017 resulted in net losses, there is no income allocation required under the two-class method or dilution attributed to pro forma weighted average shares outstanding in the calculation of pro forma diluted loss per share attributable to common stockholders.

Basic and diluted earnings per share is calculated as follows:

	Year Ended December 31,		Six Months Ended June 30,	
	2015	2016	2016	2017
Numerator:				
Net loss	\$ (11,073)	\$ (25,872)	\$ (11,115)	\$ (13,162)
Cumulative dividends on convertible preferred shares	(927)	(3,202)	(1,596)	(2,372)
Loss attributable to common shares—basic and diluted	<u>\$ (12,000)</u>	<u>\$ (29,074)</u>	<u>\$ (12,711)</u>	<u>\$ (15,534)</u>
Denominator:				
Weighted-average number of common shares—basic and diluted	10,196,292	10,196,292	10,196,292	10,196,292
Loss per common share—basic and diluted	\$ (1.18)	\$ (2.85)	\$ (1.25)	\$ (1.52)

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

**(including data applicable to unaudited periods)
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2. Summary of Significant Accounting Policies (Continued)

Pro forma earnings per share is computed as follows:

	Year Ended December 31, 2016	Six Months Ended June 30, 2017
Numerator:		
Net loss attributable to common shares—basic and diluted	\$ (25,872)	\$ (13,162)
Add: Cumulative dividends on convertible preferred shares	<u>—</u>	<u>—</u>
Net loss attributable to common stockholders—basic and diluted	<u>\$ (25,872)</u>	<u>\$ (13,162)</u>
Denominator:		
Weighted average common shares outstanding—basic and diluted	10,196,292	10,196,292
Add: Assumed conversion of convertible preferred stock to common stock	4,362,050	6,533,195
Pro forma weighted-average shares outstanding	<u>14,558,342</u>	<u>16,729,487</u>
Pro forma net loss per share—basic and diluted	<u>\$ (1.78)</u>	<u>\$ (0.79)</u>

Patent Costs

Costs to secure and defend patents are expensed as incurred and are classified as general and administrative expenses. Patent costs were \$280 and \$231 for the years ended December 31, 2015 and 2016 and \$137 and \$117 for the six months ended June 30, 2016 and 2017, respectively.

Application of New or Revised Accounting Standards

From time to time, new accounting pronouncements are issued by the FASB and adopted by the Company as of the specified effective date. Unless otherwise discussed, the Company believes that the impact of recently issued standards that are not yet effective will not have a material impact on its financial position or results of operations upon adoption.

In April 2012, the Jump-Start Our Business Startups Act (the "JOBS Act") was signed into law. The JOBS Act contains provisions that, among other things, reduce certain reporting requirements for an "emerging growth company." As an emerging growth company, the Company elected to not take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards, and as a result, will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies.

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

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2. Summary of Significant Accounting Policies (Continued)

In August 2014, the FASB issued ASU No. 2014-15, Presentation of Financial Statements—Going Concern ("ASU No. 2014-15"). The new guidance addresses management's responsibility to evaluate whether there is substantial doubt about an entity's ability to continue as a going concern and to provide related footnote disclosures. Management's evaluation should be based on relevant conditions and events that are known and reasonably knowable at the date that the financial statements are issued. This standard is effective for the annual period ending after December 15, 2016 and for the annual periods and interim periods thereafter. The Company adopted ASU 2014-15 for the year ended December 31, 2016. Refer to Note 1, Nature of Business—Liquidity for further discussion.

In November 2015, the FASB issued Accounting Standards Update No. 2015-17, *Income Taxes (Topic 740)* ("ASU 2015-17"). ASU 2015-17 requires deferred tax liabilities and assets to be classified as noncurrent in a classified statement of financial position, instead of separating deferred income tax liabilities and assets into current and noncurrent amounts. The amendments under ASU 2015-17 apply to all entities that present a classified statement of financial position and are effective, for public entities, for financial statements issued for annual periods beginning after December 15, 2016, and interim periods within those annual periods, with early adoption permitted for all entities as of the beginning of an interim or annual reporting period. The Company elected to early adopt ASU 2015-17 effective December 31, 2016. Adoption of this ASU resulted in a retrospective reclassification but did not have an impact on the Company's Balance Sheets as of December 31, 2015 and 2016.

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842). ASU 2016-02 requires lessees to recognize lease assets and lease liabilities for those leases classified as operating leases under previous GAAP. A lessee should recognize in the statement of financial position a liability to make lease payments (the lease liability) and a right-of-use asset representing its right to use the underlying asset for the lease term. For leases with a term of 12 months or less, a lessee is permitted to make an accounting policy election by class of underlying asset not to recognize lease assets and lease liabilities. The recognition, measurement, and presentation of expenses and cash flows arising from a lease by a lessee have not significantly changed from previous GAAP. There continues to be a differentiation between finance leases and operating leases. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018, and interim periods within those fiscal years, and early adoption is permitted. The Company is currently in the process of evaluating the impact of adoption of ASU No. 2016-02 on its financial position and results of operations.

In March 2016, the FASB issued ASU 2016-09, *Improvements to Employee Share-Based Payment Accounting (Topic 718)* that changes the accounting for certain aspects of share-based payments to employees. The guidance requires the recognition of the income tax effects of awards in the income statement when the awards vest or are settled, thus eliminating additional paid in capital pools. The guidance also allows for the employer to repurchase more of an employee's shares for tax withholding purposes without triggering liability accounting. In addition, the guidance allows for a policy election to account for forfeitures as they occur rather than on an estimated basis. The guidance is effective for annual periods beginning after December 15, 2016, and interim periods within those annual periods with early adoption permitted. Accordingly, the standard is effective for the Company on January 1, 2018. The

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

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2. Summary of Significant Accounting Policies (Continued)

Company adopted the standard as of January 1, 2017. The adoption did not have a material impact on the Company's financial position, results of operations or cash flows.

In November 2016, the FASB issued ASU No. 2016-18, Statement of Cash Flows (Topic 230): Restricted Cash ("ASU 2016-18") that changes the presentation of restricted cash and cash equivalents on the statement of cash flows. Restricted cash and restricted cash equivalents will be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. This amendment is effective for fiscal years beginning after December 15, 2017, including interim periods within those fiscal years. Early adoption is permitted, including adoption in an interim period. The Company is currently evaluating the impact of this new pronouncement on its statements of cash flows.

In May 2017, the FASB issued ASU 2017-09, Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting, ('ASU 2017-09'). ASU 2017-09 provides clarity and reduces both (1) diversity in practice and (2) cost and complexity when applying the guidance in Topic 718, to a change to the terms or conditions of a share-based payment award. The amendments in ASU 2017-09 should be applied prospectively to an award modified on or after the adoption date. This ASU is effective for fiscal years, and interim periods within those years, beginning after December 15, 2017. The adoption of this ASU is not expected to have a material impact on the Company's financial position or results of operations.

In July 2017, the FASB issued ASU 2017-11, Earnings Per Share (Topic 260), Distinguishing Liabilities from Equity (Topic 480) and Derivatives and Hedging (Topic 815): I. Accounting for Certain Financial Instruments with Down Round Features; II. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception, ('ASU 2017-11'). Part I of this update addresses the complexity of accounting for certain financial instruments with down round features. Down round features are features of certain equity-linked instruments (or embedded features) that result in the strike price being reduced on the basis of the pricing of future equity offerings. Current accounting guidance creates cost and complexity for entities that issue financial instruments (such as warrants and convertible instruments) with down round features that require fair value measurement of the entire instrument or conversion option. Part II of this update addresses the difficulty of navigating Topic 480, Distinguishing Liabilities from Equity, because of the existence of extensive pending content in the FASB Accounting Standards Codification. This pending content is the result of the indefinite deferral of accounting requirements about mandatorily redeemable financial instruments of certain nonpublic entities and certain mandatorily redeemable noncontrolling interests. The amendments in Part II of this update do not have an accounting effect. This ASU is effective for fiscal years, and interim periods within those years, beginning after December 15, 2018. The Company is currently assessing the potential impact of adopting ASU 2017-11 on its financial statements and related disclosures.

Subsequent Events

The Company considers events or transactions that occur after the balance sheet date but prior to the issuance of the financial statements to provide additional evidence for certain estimates or to identify

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

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2. Summary of Significant Accounting Policies (Continued)

matters that require additional disclosure. Subsequent events have been evaluated as required. See Note 12.

3. Accrued Expenses

Accrued expenses consisted of the following:

	December 31,	June 30
	<u>2015</u>	<u>2016</u>
Research and development costs	\$ 998	\$ 2,049
Professional fees	1,920	182
Payroll related	—	344
Other	44	80
Accrued expenses	\$ 2,962	\$ 2,655
	<u>\$ 3,470</u>	<u>\$ 3,470</u>

4. Preferred Stock

In August 2015, pursuant to the Series A Preferred Stock Purchase Agreement, by and among the Company and certain purchasers, and as part of an initial tranche closing, the Company issued 25,000,000 shares of Series A Convertible Preferred Stock, par value \$0.001 per share, at a purchase price of \$1.00 per share, resulting in net proceeds of \$24,976 to the Company (the "August 2015 Initial Tranche Closing"). The Series A Preferred Stock Purchase Agreement provided for the delayed issuance of up to an additional 15,000,000 shares of Series A Convertible Preferred Stock as part of a Second Tranche Closing. The delayed issuance was to be automatically settled upon the achievement of a specific milestone, resulting in the issuance of shares of Series A Convertible Preferred Stock (the "2015 Series A Investor Right/Obligation"). The 2015 Series A Investor Call Option would become exercisable in the event that a Second Tranche Closing was not been consummated. Both the 2015 Series A Investor Right/Obligation and the 2015 Series A Investor Call Option were evaluated and determined to be free standing instruments and were being accounted as liabilities (see Note 2). In December 2015, the specific milestones were met and 15,000,000 shares of Series A Convertible Preferred Stock were issued at a purchase price of \$1.00 per share for net proceeds of \$14,641. The 2015 Series A Investor Call Option expired unexercised at that time.

In January 2017, pursuant to the Series A Preferred Stock Purchase Agreement, by and among the Company and certain purchasers, and as part of an initial tranche closing, the Company issued 20,475,001 shares of Series A Convertible Preferred Stock, par value \$0.001 per share, at a purchase price of \$1.00 per share, resulting in net proceeds of \$20,377 to the Company (the "January 2017 Initial Tranche Closing"). The Series A Preferred Stock Purchase Agreement provided for the delayed issuance by the Company of up to an additional 20,474,998 shares of Series A Convertible Preferred Stock as part of a second tranche closing at a purchase price of \$1.00 per share (the "2017 Series A Investor Right/Obligation"). The second tranche is contingent upon: (1) the Company's cash, cash equivalents and short-term investments balance, net of accounts payable and accrued liabilities, falling below \$5.0 million and (2) the Company's

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

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4. Preferred Stock (Continued)

satisfaction of contractual and customary representations and warranties. Unless otherwise mutually agreed upon in writing, the rights and obligations underlying the second tranche (if not previously executed) will terminate on the first to occur of the following dates: (1) the date (the "Roadshow Acceleration Date") on which the Company files with the SEC the last pre-effective amendment to the Registration Statement prior to the start of the Company's roadshow in connection with the IPO, provided, that such termination shall be contingent upon the consummation of the IPO pursuant to the same Registration Statement that was on file with the SEC on the Roadshow Acceleration Date, without withdrawal thereof or filing of a subsequent Registration Statement in replacement thereof; and (2) the date of the consummation of a Deemed Liquidation Event (as defined below). To the extent the closing of the second tranche has not already taken place, the investors in the first tranche also have a call right on the shares underlying the second tranche whereby such shares can be purchased for the same price as the second tranche (the "2017 Series A Investor Call Option"). The 2017 Series A Investor Call Option terminates upon the Roadshow Acceleration Date. The 2017 Series A Investor Right/Obligation and the 2017 Series A Investor Call Option have been evaluated and determined to be a free standing instrument, the 2017 Series A Investor Instrument. The 2017 Series A Investor Instrument is being accounted for as a liability (see Note 2). In August 2017, the Series A Investors waived the \$5.0 million cash balance requirement of the Series A Investor Right/Obligation and closed the second tranche of the series A preferred stock financing (see Note 12 for further discussion).

Upon the closing of an initial public offering with a minimum price per share and gross proceeds of at least \$1.00, as adjusted for any splits or similar changes, and \$50.0 million, respectively, the Series A Convertible Preferred Stock will automatically convert into shares of Common Stock on a 9.17-for-1 basis.

The holders of the Series A Convertible Preferred Stock have the following rights and preferences:

Voting Rights

The holders of Series A Convertible Preferred Stock are entitled to vote, together with the holders of Common Stock, on all matters submitted to stockholders for a vote. Each preferred stockholder is entitled to the number of votes equal to the number of shares of Common Stock into which each preferred share is convertible at the time of such vote. In addition, pursuant to the Company's charter, the holders of record of the outstanding shares of Series A Convertible Preferred Stock are entitled to elect one director to serve as the Series A Preferred Director on the board of directors of the Company.

Dividends

The holders of Series A Convertible Preferred Stock are entitled to receive dividends in preference to any dividend on Common Stock at the rate of 8.0% per year of the original issue price. Dividends shall accrue annually, whether or not declared, and shall be cumulative. The Company may not declare, pay or set aside any dividends on shares of any other class or series of capital stock of the Company unless the holders of Series A Convertible Preferred Stock then outstanding shall first receive, or simultaneously receive, dividends on each outstanding share of Series A Convertible Preferred Stock. Through December 31, 2016 and June 30, 2017, no dividends had been declared or paid by the Company. Accrued dividends, whether or not declared, shall also be payable upon any liquidation event. At December 31,

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4. Preferred Stock (Continued)

2016 and June 30, 2017, cumulative preference dividends amounted to \$4,129, or \$0.10 per share and \$6,502, or \$0.11 per share, respectively.

Liquidation

In the event of any liquidation, dissolution or winding-up of the Company or a Deemed Liquidation Event (as defined below), the holders of Series A Convertible Preferred Stock then outstanding shall be entitled to be paid out of the assets of the Company available for distribution to stockholders, and before any payment shall be made to holders of Common Stock, an amount per share equal to greater of (i) the original issue price per share, plus any accrued but unpaid dividends thereon, whether or not declared, plus any declared but unpaid dividends thereon, if any, or (ii) such amount per share as would have been payable had all shares of Series A Convertible Preferred Stock been converted to Common Stock prior to such liquidation. If upon such event, the assets of the Company available for distribution are insufficient to permit payment in full to the holders of Series A Convertible Preferred Stock, the proceeds will be ratably distributed among the holders of Series A Convertible Preferred Stock in proportion to the respective amounts that they would have received if they were paid in full. After payments have been made in full to the holders of Series A Convertible Preferred Stock, the remaining assets of the Company available for distribution will be distributed among the holders of Series A Convertible Preferred Stock and the holders of Common Stock as if the shares of Series A Convertible Preferred Stock were converted to Common Stock immediately prior to the liquidation event.

A merger, acquisition, sale of voting control or other transaction of the Company in which the stockholders of the Company do not own a majority of the outstanding shares of the surviving company shall be considered a Deemed Liquidation Event. A sale, exclusive license, transfer or other disposition of all or substantially all of the assets of the Company shall also be considered a Deemed Liquidation Event. Each share of Series A Convertible Preferred Stock may be redeemed at the option of the holder upon the occurrence of a deemed liquidation event. As of December 31, 2015 and 2016 and June 30, 2017, the liquidation preference of the outstanding shares of Series A Convertible Preferred Stock was approximately \$40,927, \$44,129 and \$66,977, respectively.

Conversion

Each share of Series A Convertible Preferred Stock is convertible into common stock at the option of the stockholder at any time after the date of issuance. In addition, each share of Series A Convertible Preferred Stock will be automatically converted into shares of common stock, at the applicable conversion ratio then in effect, upon the earlier of (i) a qualified public offering with gross proceeds of at least \$50,000 and a price of not less than \$1.00 per share, subject to appropriate adjustment for any stock dividend, stock split, combination or other similar recapitalization, and (ii) the date specified by vote or written consent of the holders of at least two-thirds of the then outstanding shares of series A preferred stock. The shares of Series A Convertible Preferred Stock will be converted to common stock, at par value, with the remainder recorded to additional paid-in capital.

The conversion ratio of the Series A Convertible Preferred Stock is determined by dividing the original issue price per share by the conversion price of \$1.00 per share, subject to appropriate adjustment

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

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4. Preferred Stock (Continued)

in the event of any stock dividend, stock split, combination or recapitalization affecting the Series A Convertible Preferred Stock. As of December 31, 2016 and June 30, 2017, the outstanding shares of Series A Convertible Preferred Stock were convertible into 4,362,050 and 6,594,874 shares of common stock, respectively.

5. Fair Value of Financial Assets and Liability

As of December 31, 2015 and 2016 and June 30, 2017, the carrying amount of cash and cash equivalents and short-term investments was \$34,869, \$10,537 and \$17,740 respectively, which approximates fair value. Cash and cash equivalents and short-term investments includes investments in money market funds that invest in U.S. government securities that are valued using quoted market prices. Accordingly, money market funds and government funds are categorized as Level 1 and had a total balance of \$11,972, \$7,984 and \$13,316 as of December 31, 2015 and 2016 and June 30, 2017, respectively.

For the years ended December 31, 2015 and 2016, the Company had no financial liabilities outstanding measured at fair value. The Company recognized a financial liability during 2015 related to its 2015 Series A Investor Right/Obligation and 2015 Series A Investor Call Option that was exercised or expired, respectively, in December 2015. The liability was based on significant inputs not observable in the market, which represents a Level 3 measurement within the fair value hierarchy. A financial liability was recognized during the six months ending June 30, 2017 related to the 2017 Series A Investor Instrument. The liability was valued based on significant inputs not observable in the market, which represents a Level 3 measurement within the fair value hierarchy.

The following tables present information about the Company's financial assets and liabilities measured at fair value on a recurring basis and indicate the level of the fair value hierarchy utilized to determine such fair values:

	Fair value Measurements as of June 30, 2017 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash Equivalents:				
Government Funds	\$ —	\$ —	\$ —	\$ —
Money Market Funds	4,299	—	—	4,299
Marketable Securities:				
Government Funds	9,017	—	—	9,017
Total	<u><u>\$ 13,316</u></u>	<u><u>\$ —</u></u>	<u><u>\$ —</u></u>	<u><u>\$ 13,316</u></u>
Liabilities:				
2017 Series A Investor Instrument	\$ —	\$ —	\$ 410	\$ 410
Total	<u><u>\$ —</u></u>	<u><u>\$ —</u></u>	<u><u>\$ 410</u></u>	<u><u>\$ 410</u></u>

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

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5. Fair Value of Financial Assets and Liability (Continued)

	Fair value Measurements as of December 31, 2016 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash Equivalents:				
Government Funds	\$ 2,000	\$ —	\$ —	\$ 2,000
Money Market Funds	1,987	—	—	1,987
Marketable Securities:				
Government Funds	3,997	—	—	3,997
Total	\$ 7,984	\$ —	\$ —	\$ 7,984

	Fair Value Measurements as of December 31, 2015 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash Equivalents:				
Government Funds	\$ 4,508	\$ —	\$ —	\$ 4,508
Money Market Funds	7,464	—	—	7,464
Liabilities:				
Series A Investor Right/Obligation and Series A Investor Call Option	\$ —	\$ —	\$ —	\$ —
Total	\$ 11,972	\$ —	\$ —	\$ 11,972

Marketable Securities

The following tables summarize the Company's marketable securities:

	June 30, 2017			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Assets				
Government Funds (due within 1 year)	\$ 9,020	\$ —	\$ (3)	\$ 9,017
	\$ 9,020	\$ —	\$ (3)	\$ 9,017
December 31, 2016				
	December 31, 2016			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Assets				
Government Funds (due within 1 year)	\$ 3,997	\$ —	\$ —	\$ 3,997
	\$ 3,997	\$ —	\$ —	\$ 3,997

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

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5. Fair Value of Financial Assets and Liability (Continued)

Below is a roll forward of the fair value of financial liabilities for the year ended December 31, 2015:

	2015 Series A Investor Right/Obligation And 2015 Series A Investor Call Option
Fair value at December 31, 2014	\$ —
Fair value upon the August 2015 Initial Closing	\$ 500
Change in fair value through the date of settlement	500
Reclassification of liability upon December 2015 Second Tranche closing	(1,000)
Fair value at December 31, 2015	<u><u>\$ —</u></u>

The following assumptions and inputs were used in determining the fair value of the 2015 Series A Investor Call Option valued using the Black- Scholes option pricing model:

	August 2015 Initial Tranche Closing
Series A Convertible Preferred Stock Exercise Price	\$1.00
Series A Convertible Preferred Stock Fair Value	\$0.81
Expected term	2 months
Expected volatility	24.0%
Expected interest rate	0.08%
Expected dividend yield	—

The 2015 Series A Investor Call Option expired upon the Second Tranche Closing in December 2015.

The Company estimated the fair value of the 2015 Series A Investor Right/Obligation as the probability-weighted present value of the expected benefit of the investment. The expected benefit is the difference between the expected future value of shares issued upon the second tranche closing and the investment price for the second tranche closing. The expected future value as of the August 2015 Initial Tranche Closing was estimated through a backsolve calculation which assumes a 70 percent probability of closing, a discount rate of 0.08% and a second tranche closing date of November 30, 2015.

The Company performed a contemporaneous valuation of the 2015 Series A Investor Right/Obligation to invest in the second tranche of our series A preferred stock financing. This valuation coincided with the 2015 Series A Second Tranche Closing on December 1, 2015. The Company valued the 2015 Series A Investor Right/Obligation as the benefit associated with the second tranche investment. The benefit is a function of the difference between the fair value of the series A shares and the 2015 Series A Investor Right/Obligation exercise price on the date of closing and the number of shares acquired. The Company estimated the fair value of the 2015 Series A Investor Right/Obligation as the probability weighted average of two scenarios: an IPO and a remain-private scenario.

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

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5. Fair Value of Financial Assets and Liability (Continued)

Below is a roll forward of the fair value of the 2017 Series A Investor Instrument for the six months ended June 30, 2017:

	2017 Series A Investor Instrument
Fair value at December 31, 2016	\$ —
Fair value upon the January 2017 Initial Closing, net	328
Change in fair value	82
Fair value at June 30, 2017, net	<u>\$ 410</u>

The fair value of the Series A Investor Instrument is the sum of the probability-weighted fair value of the 2017 Investor Right/Obligation and the 2017 Series A Call Option.

The following assumptions and inputs were used in determining the fair value of the 2017 Series A Investor Call Option valued using the Black-Scholes option pricing model:

	June 30, 2017
Series A Convertible Preferred Stock Exercise Price	\$1.00
Series A Convertible Preferred Stock Fair Value	\$1.30
Expected term	3.5 months
Expected volatility	72.0%
Expected interest rate	1.03%
Expected dividend yield	—

The Company estimated the fair value of the 2017 Series A Investor Right/Obligation as the probability-weighted present value of the expected benefit of the investment. The expected benefit is the difference between the expected future value of shares issued upon the second tranche closing and the investment price for the second tranche closing. The expected future value is estimated as a weighted average of IPO and remain private scenarios, and the future value is converted to a present value assuming a closing date of August 15, 2017 and a nominal, risk-free discount rate.

6. Common Stock

In March 2013, the Company issued 10,196,292 shares of common stock at a purchase price of \$0.001 per share. As of December 31, 2015 and 2016 and June 30, 2017, the LLC entity owned all of these shares.

In August 2015, the Company's board of directors approved a 93,500-for-one forward stock split of the Company's issued and outstanding shares of common stock. The Company filed an amended and restated certificate of incorporation with the Secretary of State of the State of Delaware to increase its authorized number of shares of common stock to 16,357,688 shares of common stock, \$0.001 par value per share, 10,196,292 shares of which were issued and outstanding as of June 30, 2017.

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

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6. Common Stock (Continued)

In January 2017, the Company filed a second amended and restated certificate of incorporation with the Secretary of State of the State of Delaware to increase its authorized number of shares of common stock to 21,341,330 shares of common stock, \$0.001 par value per share. The Company has reserved 2,317,339 shares of common stock for issuance to officers, directors, employees and consultants of the Company pursuant to the 2015 Stock Incentive Plan (the "2015 Plan") duly adopted by the Company's board of directors and approved by the Company's stockholders. Of such reserved shares of common stock, as of June 30, 2017 no shares have been issued pursuant to restricted stock purchase agreements, 1,433,262 options to purchase shares of common stock have been granted, and 884,077 shares of common stock remain available for issuance to officers, directors, employees and consultants pursuant to the 2015 Plan.

In August 2017, the Company filed an amended and restated certificate of incorporation with the Secretary of State of the State of Delaware to increase its authorized number of shares of common stock to 29,919,979 shares of common stock, \$0.001 par value per share.

In connection with the offering, the Company will effect a 1-for-9.17 reverse stock split for our then outstanding common stock. All shares and per share amounts in the financial statements have been retrospectively adjusted for all periods presented to give effect of the reverse stock split.

7. Stock-based Compensation**2015 Stock Incentive Plan****2015 Plan Overview**

In August 2015, the Company's board of directors approved the 2015 equity incentive plan, as amended and in effect prior to the closing of this offering, or the 2015 Plan, which provides for the grant of incentive and non-qualified stock options and restricted stock awards to employees, consultants, advisors and directors, as determined by the board of directors. The Company reserved 2,317,339 shares of common stock to be issued under the 2015 Plan. Shares of common stock issued upon exercise of stock options are generally issued from new shares of the Company. The 2015 Plan provides that the exercise price of incentive stock options cannot be less than 100% of the fair market value of the common stock on the date of the award for participants who own less than 10% of the total combined voting power of stock of the Company, and not less than 110% for participants who own more than 10% of the Company's voting power. Options and restricted stock granted under the 2015 Plan will vest over periods as determined by the Company's board of directors. For options granted to date, the exercise price equaled the fair value of the common stock as determined by the board of directors on the date of grant.

The Company estimates the fair value of stock-based awards to employees and non-employees using the Black-Scholes option-pricing model, which requires the input of highly subjective assumptions, including (a) the expected volatility of the underlying common stock, (b) the expected term of the award, (c) the risk-free interest rate, and (d) expected dividends. Due to the lack of a public market for the trading of its common stock and a lack of company-specific historical and implied volatility data, the Company

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

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7. Stock-based Compensation (Continued)

based its estimate of expected volatility on the historical volatility of a group of companies in the pharmaceutical and biotechnology industries in a similar stage of development as the Company that are publicly traded. For these analyses, the Company selected companies with comparable characteristics to its own including enterprise value, risk profiles and with historical share price information sufficient to meet the expected life of the stock-based awards. The Company computes the historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of its stock-based awards. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available. The Company estimated the expected life of its employee stock options using the "simplified" method, whereby, the expected life equals the average of the vesting term and the original contractual term of the option. The risk-free interest rates for periods within the expected life of the option are based on the U.S. Treasury yield curve in effect during the period the options were granted.

The Company is also required to estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from estimates. The Company used historical data to estimate pre-vesting option forfeitures and record stock-based compensation expense only for those awards that are expected to vest. To the extent that actual forfeitures differ from its estimates, the difference is recorded as a cumulative adjustment in the period the estimates were revised. Stock-based compensation expense recognized in the financial statements is based on awards that are ultimately expected to vest. Upon adopting ASU 2016-09 on January 1, 2017, the Company elected to account for forfeitures as they occur.

The grant date fair value of awards subject to service-based vesting, net of estimated forfeitures, is recognized ratably over the requisite service period, which is generally the vesting period of the respective awards. The Company's stock option awards typically vest over a service period that ranges from three to four years and includes awards with one year cliff vesting followed by ratable monthly vesting thereafter and ratable monthly vesting beginning on the grant date.

The unvested portion of stock options granted to non-employees are subject to remeasurement at subsequent reporting periods.

2017 Activity

During the six months ended June 30, 2017, the Company granted 483,369 common stock option awards to certain directors, employees and non-employees.

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

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7. Stock-based Compensation (Continued)

The fair value of share options granted during the six months ended June 30, 2017 was estimated using the Black-Scholes option pricing model with the following weighted-average assumptions:

	Six Months Ended June 30, 2017
Risk-free interest rate	2.00%
Expected term (in years)	6.03
Expected volatility	66.28%
Expected dividend yield	—

2016 Activity

During the year ended December 31, 2016, the Company granted 164,231 common stock option awards to certain of its employees and non-employees.

The fair value of share options granted to employees during the year ended December 31, 2016 was estimated using the Black-Scholes option pricing model with the following weighted-average assumptions:

	Year ended December 31, 2016
Risk-free interest rate	1.39%
Expected term (in years)	6.25
Expected volatility	74.20%
Expected dividend yield	—

The fair value of share options granted to non-employees during the year ended December 31, 2016 was estimated using the Black-Scholes option pricing model with the following weighted-average assumptions:

	Year ended December 31, 2016
Risk-free interest rate	1.58%
Expected term (in years)	10.0
Expected volatility	71.18%
Expected dividend yield	—

2015 Activity

During 2015, the Company granted 900,165 common stock option awards to certain of its employees and non-employees. Of the awards granted, 655,599 were to Motus employees providing service to the

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

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7. Stock-based Compensation (Continued)

Company through a service arrangement (See Note 2). As Motus and the Company are under the common control of the LLC entity, the awards are treated as a dividend to the LLC entity for the Company's standalone financial reporting in accordance with ASC 718, Compensation—Stock Compensation. The grant date fair value of \$2,695 for the grants was established using a Black-Scholes model with assumptions consistent with ASC 505-50, Equity-Based Payments to Non-employees and was recorded as a dividend with a corresponding credit to Additional Paid-in Capital. As Motus is recognizing these grants to its employees as compensation expense on a fair value basis in accordance with ASC 815, Derivatives and Hedging, the Company is recognizing its proportionate share of the compensation expense recognized by Motus consistent with its accounting policy described in Note 2.

On November 16, 2016, the Motus employees terminated their employment contracts with Motus and entered into new employment agreements with the Company. The fair value of the remaining unvested awards for these employees will be expensed in accordance with ASC 718, Compensation—Stock Compensation over their remaining vesting period.

The fair value of share options granted to employees and directors during the year ended December 31, 2015 was estimated using the Black-Scholes option pricing model with the following weighted-average assumptions:

	Year Ended December 31, 2015
Risk-free interest rate	1.84%
Expected term (in years)	5.93
Expected volatility	66.5%
Expected dividend yield	—

The fair value of share options granted to non-employees during the year ended December 31, 2015 was estimated using the Black-Scholes option pricing model with the following weighted-average assumptions:

	Year Ended December 31, 2015
Risk-free interest rate	2.25%
Expected term (in years)	10.0
Expected volatility	75.7%
Expected dividend yield	—

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

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7. Stock-based Compensation (Continued)

A summary of the Company's common stock option activity for the year ended December 31, 2016 and six months ended June 30, 2017 is as follows:

	Number of Units	Weighted-Average Grant Date Fair Value Per Unit	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term
Outstanding as of December 31, 2015	900,165	\$ 3.76	\$ 5.04	9.90
Granted	164,231	4.59	6.79	—
Exercised	—	—	—	—
Cancelled	—	—	—	—
Outstanding as of December 31, 2016	1,064,396	3.94	5.32	9.02
Granted	483,369	3.76	6.14	—
Exercised	—	—	—	—
Cancelled	(114,503)	(4.59)	(6.88)	—
Outstanding as of June 30, 2017	1,433,262	\$ 3.76	\$ 5.50	8.87
Options vested and expected to vest as of December 31, 2016	<u>1,064,396</u>	<u>\$ 3.94</u>	<u>\$ 5.32</u>	9.02
Options vested and expected to vest as of June 30, 2017	<u>1,378,737</u>	<u>\$ 3.76</u>	<u>\$ 5.41</u>	8.84
Options exercisable at December 31, 2016	<u>310,107</u>	<u>\$ 3.85</u>	<u>\$ 5.04</u>	8.90
Options exercisable at June 30, 2017	<u>453,400</u>	<u>\$ 3.85</u>	<u>\$ 5.23</u>	8.52

Under the 2015 Plan, the Company recorded stock-based compensation of \$192 and \$993 during the year ended December 31, 2015 and 2016, respectively, that consists of stock-based compensation expense for stock options granted to employees and Company directors of \$39 and \$277, respectively and stock options granted to non-employees and employees of the Motus entity that are allocated to the Company of \$153 and \$716, respectively.

Stock compensation expense incurred under the 2015 Plan was \$473 and \$627 during the six months ended June 30, 2016 and 2017, respectively, consisting of stock-based compensation expense for awards granted to employees and our directors of \$100 and \$581, respectively, and non-employees and, for the six months ended June 30, 2016, employees of the Relamorelin Company that were allocated to us of \$373 and \$46, respectively. As of December 31, 2016 and June 30, 2017, the Company has unrecognized compensation cost of \$2,826 and \$3,622, respectively, related to non-vested employee, non-employee and director awards that is expected to be recognized over a weighted-average period of 2.78 years and 2.65 years, respectively.

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

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7. Stock-based Compensation (Continued)

The following table summarizes the classification of the Company's stock-based compensation expenses related to the 2015 Plan recognized in the Company's statements of operations and comprehensive loss.

	Year Ended December 31,		Six Months Ended June 30,	
	2015	2016	2016	2017
Research and development	\$ 68	\$ 343	\$ 152	\$ 190
General and administrative	124	650	321	437
Total	<u>\$ 192</u>	<u>\$ 993</u>	<u>\$ 473</u>	<u>\$ 627</u>

LLC Incentive Plan

The Company was allocated stock compensation expense from the LLC entity's plan using the same proportional use basis for other shared costs (see Note 2). The following table summarizes the classification of the Company's stock-based compensation expenses related to the costs allocated from the LLC's Plan recognized in the Company's statements of operations and comprehensive loss.

	Year Ended December 31,		Six Months Ended June 30,	
	2015	2016	2016	2017
Research and development	\$ 76	\$ 163	\$ 78	\$ 71
General and administrative	30	12	8	—
Total	<u>\$ 106</u>	<u>\$ 175</u>	<u>\$ 86</u>	<u>\$ 71</u>

The remainder of this Note discloses the stock-based compensation activity of the Predecessor Company and the LLC entity.

Original Plan

The Predecessor Company had one stock based compensation plan—the 2010 equity incentive plan, as amended (the "Original Plan"). The Original Plan previously provided for the grant of incentive and non-qualified stock options and restricted stock grants to employees, consultants, advisors and directors, as determined by the board of directors of the Predecessor Company.

As a result of the Corporate Reorganization, all outstanding option grants under the Original Plan were cancelled. Each holder of a stock option that was cancelled was issued a restricted common unit of the LLC entity in its place on a 1-for-1 basis. Restricted common unit vesting agreements were contracted between the LLC entity and the restricted common unit holder granting the holder the same vesting terms.

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

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7. Stock-based Compensation (Continued)

as originally granted in the respective option agreement. Any unvested portion of the stock option at the Corporate Reorganization would continue to vest under those original time frames and conditions. Exercise prices were eliminated as they are not applicable to common unit instruments, and all equity incentive grants after the Corporate Reorganization were of restricted common units.

The holder of a restricted common unit is entitled to one vote per unit. After the payment of all preferential amounts to the holders of the convertible preferred units, the holder of a restricted common unit is entitled to his pro rata share of the remaining consideration, if any, based on the number of restricted common units held by the holder.

Restricted Common Units

Upon the Corporate Reorganization, all 615,685 common stock options of the Predecessor Company under the Original Plan outstanding as of March 21, 2013 were exchanged on a 1-for-1 basis for 615,685 restricted common units of the LLC entity. Vesting continued on the same schedule as originally granted per the respective option agreement. At the time of the exchange, the LLC entity determined the fair value of a restricted common unit to be \$1.21 per unit, equivalent to the fair value of a common unit. The fair value of stock options immediately prior to the Corporate Reorganization was determined using a Black-Scholes option pricing model and ranged in value from \$0.48 to \$0.64. The exchange was accounted for by the LLC entity as a modification in accordance with ASC 718, with the incremental fair value determined to be \$255, of which \$99 was recognized immediately upon the Corporate Reorganization for the portion related to the vested awards, and the remaining \$156 will be recognized over the remaining service period of the restricted common units, net of estimated forfeitures. No common stock options were issued by the Relamorelin Company under the Original Plan subsequent to the Corporate Reorganization.

All restricted common units granted subsequent to the Corporate Reorganization were valued at the fair value of the LLC entity's common unit on the date of grant and will be expensed over their respective service period. Forfeitures are required to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. The term "forfeitures" is distinct from "cancellations" and represents only the unvested portion of the surrendered unit. Ultimately, the actual expense recognized over the vesting period will only be for those options that vest.

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

**(including data applicable to unaudited periods)
(Information as of June 30, 2017 and for the
six months ended June 30, 2016 and 2017 is unaudited)**

(In thousands, except share and per share information)

7. Stock-based Compensation (Continued)

A summary of the LLC entity's restricted common unit activity for the year ended December 31, 2016 and the six months ended June 30, 2017 is as follows:

	Number of Units	Weighted-Average Grant Date Fair Value Per Unit
Outstanding unvested as of December 31, 2015	145,413	\$ 3.59
Granted	—	—
Vested	(50,796)	4.10
Cancelled	—	—
Outstanding unvested as of December 31, 2016	94,617	\$ 3.31
Granted	—	—
Vested	(14,124)	5.06
Cancelled	—	—
Outstanding unvested as of June 30, 2017	<u>80,493</u>	<u>\$ 3.01</u>

The LLC entity recorded total stock-based compensation expense for restricted common units granted to employees, directors and non-employees of \$337 and \$221 during the years ended December 31, 2015 and 2016, respectively and \$108 and \$71 for the six months ended June 30, 2016 and 2017, respectively. The total fair value of restricted common units vested during the years ended December 31, 2015 and 2016 and six months ended June 30, 2017 was \$309, \$208 and \$71, respectively. As of December 31, 2016 and June 30, 2017, we have unrecognized compensation expense related to the unvested portion of these awards of \$314 and \$242, respectively, and we expect to recognize this amount over a weighted-average period of approximately 1.8 years and 1.31 years, respectively.

Restricted Common Unit Grants to Non-Employees

During the years ended December 31, 2015, subsequent to the Corporate Reorganization, the LLC entity granted restricted common units to non-employee consultants. The LLC entity valued these restricted common units based on their fair value on the date of grant, determined to be the fair value of a common unit.

The unvested restricted common units held by consultants have been and will be remeasured using the LLC entity's estimate of fair value at each reporting period through the remaining vesting period. As of December 31, 2016, the restricted common units held by consultants have been vested. Stock-based compensation expense of \$47 and \$57 was recorded for the years ended December 31, 2015 and 2016, respectively, relating to non-employee unit awards.

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

**(including data applicable to unaudited periods)
(Information as of June 30, 2017 and for the
six months ended June 30, 2016 and 2017 is unaudited)**

(In thousands, except share and per share information)

8. Significant Agreements***License Agreements***

The Predecessor Company entered into a license agreement on February 26, 2010 with Ipsen Pharma, S.A.S. ("Ipsen") that granted full worldwide right for two programs that include the clinical candidates setmelanotide, which is in Phase 2 clinical trials, and relamorelin, which has completed a Phase 2 clinical trial. As a result of the Corporate Reorganization described in Note 1, the Ipsen license was converted to separate license agreements for the setmelanotide program held by the Company and the relamorelin program held by the Relamorelin Company, respectively. Under the terms of the setmelanotide Ipsen license agreement, assuming that setmelanotide is successfully developed, receives regulatory approval and is commercialized, Ipsen may receive aggregate payments of up to \$40,000 upon the achievement of certain development and commercial milestones and royalties on future product sales in the mid-single digits. Substantially all of such aggregate payments of up to \$40,000 are for milestones that may be achieved no earlier than first commercial sale of setmelanotide. In the event that the Company executes a sublicense agreement, it shall make payments to Ipsen, depending on the date of such sublicense agreement, ranging from 10% to 20% of all revenues actually received under such sublicense agreement.

In connection with this license agreement, the LLC entity issued two warrants in March 2010 to an affiliate of Ipsen to purchase a total of 489,500 common units. These warrants were vested in full in 2010 and 2011, respectively. In July 2015, the warrant agreement was amended to extend the expiration date to July 31, 2015 as the original warrant agreement expired in March 2015. In July 2015, an affiliate of Ipsen elected to exercise these warrants in full for a total of 489,500 common units of the LLC entity. In July 2015, upon exercise, warrant expense of \$923 was allocated to the Company relating to the modification of these warrants and is included within research and development expense.

In January 2016, the Company entered into a licensing agreement with Camurus AB, or Camurus, for the use of Camurus' drug delivery technology. The contract includes a non-refundable and non-creditable signing fee of \$500, which was paid during January 2016. The Camurus Agreement also includes up to \$7,750 in one-time, non-refundable development milestones achievable upon certain regulatory successes. The Company is also required to pay to Camurus royalties, mid to mid-high single digit, on a product-by-product and country-by-country basis of annual net sales, until the later of (i) 10 years after the date of first commercial sale of such product in such country; or (ii) the expiration of the last to expire valid claim of all licensed patent rights in such country covering such product. The Company is also required to pay one-time, non-refundable, non-creditable sales milestones upon the achievement of certain sales levels for such product and cannot be in excess of \$57,000.

In March 2017, the Company achieved the first milestone event associated with this license agreement. The Company completed the first manufactured batch using the Camurus drug delivery technology and filed an investigational new drug application with the FDA. The fee associated with this milestone was \$250.

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

**(including data applicable to unaudited periods)
(Information as of June 30, 2017 and for the
six months ended June 30, 2016 and 2017 is unaudited)**

(In thousands, except share and per share information)

9. Commitments and Contingencies

The Company is not a party to the lease for the facility it previously shared with the Relamorelin Company. In November 2015, the Company entered into a Lease Agreement for an office facility at 500 Boylston Street, Boston, Massachusetts. The lease term commenced in May 2016 and has a term of 5 years with a five -year renewal option to extend the lease. Rent expense for the years ended December 31, 2015 and 2016 and the six months ended June 30, 2017 was zero, \$179 and \$107, respectively.

Future minimum payments under the operating lease agreements as of December 31, 2016, are as follows:

2017	\$ 291
2018	298
2019	305
2020	311
2021	131
Total	<u>\$ 1,336</u>

10. Related-Party Transactions

The Company shared costs with the Relamorelin Company, its affiliate, including payroll, facilities, information technology and other research and development and general and administrative overhead costs. Additionally, the Relamorelin Company had paid certain Company expenses directly on behalf of the Company. Shared costs incurred by the Relamorelin Company and Company expenses paid by the Relamorelin Company on behalf of the Company are allocated from the Relamorelin Company to the Company as described in Note 1 and Note 2. These net costs totaled \$2,149 and \$1,570 for the years ended December 31, 2015 and 2016, respectively. From August 1, 2015 to December 31, 2015, Company expenses paid by the Relamorelin Company on behalf of the Company amounted to \$1,416 of which \$781 were repaid by the Company and \$635 were recorded as a liability within Due to related party on the balance sheet as of December 31, 2015. Prior to August 1, 2015, these amounts were recorded by the Company within Additional Paid-in Capital as capital contributions from the LLC entity as such amounts are not repayable from the Company to the Relamorelin Company or the LLC entity. Prior to August 1, 2015, these capital contributions were recorded as financing activities in the statements of cash flows. Beginning on August 1, 2015 the liabilities due to Relamorelin Company were recorded as operating activities in the statements of cash flows, as they are fully repayable and relate to the Company's operating costs. Cash transfers to the Company from the LLC entity totaled \$1,595 for the years ended December 31, 2015. There were no cash transfers in the period from August 1, 2015 to December 31, 2016. These amounts have been recorded by the Company within Additional Paid-in Capital as capital contributions from the LLC entity as such amounts are not repayable from the Company to the Relamorelin Company or the LLC entity. As of December 31, 2015, these capital contributions totaled \$42,462. The Relamorelin Company was sold to a large pharmaceutical company on December 15, 2016.

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

**(including data applicable to unaudited periods)
(Information as of June 30, 2017 and for the
six months ended June 30, 2016 and 2017 is unaudited)**

(In thousands, except share and per share information)

10. Related-Party Transactions (Continued)

The Company made payments on behalf of the LLC entity totaling \$60 related to third party services to an unaffiliated vendor. Those costs are capitalized as a receivable due from the LLC entity to the Company at December 31, 2015 on the balance sheet. There were no such payments by the Company during 2016. The LLC made payments on behalf of the Company totaling \$105 related to allocated 2016 employee bonuses. Those costs are recorded as a payable due to the LLC entity from the Company at December 31, 2016 on the balance sheet.

Expenses paid directly by the Company to consultants considered to be related parties amounted to \$153, \$619, \$202 and \$586 for the year ended December 31, 2015 and 2016 and the six months ended June 30, 2016 and 2017, respectively. Outstanding payments due to these related parties as of December 31, 2015 and 2016 and June 30, 2017 were \$13, \$50 and \$89, respectively and were included within Accounts payable on the balance sheet. Expenses paid by the Relamorelin Company to these related parties amounted to \$1,357, \$966, \$449 and zero for the year ended December 31, 2015 and 2016 and the six months ended June 30, 2016 and 2017, respectively. Outstanding payments due by the Relamorelin Company on the Company's behalf to these related parties as of December 31, 2015 and 2016 were \$58 and zero, respectively.

Employees of certain holders of series A and series B convertible preferred units of the LLC entity, have been retained as consultants supporting development activities of the Company and the Relamorelin Company for which the holders are paid cash compensation pursuant to consulting arrangements. Compensation payments related to these consultants totaled \$125, \$78, \$37 and \$44 for the years ended December 31, 2015 and 2016 and the six months ended June 30, 2016 and 2017, respectively.

11. Income Tax

In the Company's financial statements, income taxes, including deferred tax balances, have been calculated on a separate tax return basis. Certain of the Company's activities and costs have been included in the tax returns filed by the Relamorelin Company and the LLC entity. Prior to the Corporate Reorganization, the Company's operations were included in the tax returns filed by the Predecessor Company. The Company has filed tax returns on its own behalf since the Corporate Reorganization.

For the years ended December 31, 2015 and 2016, the Company did not have a current or deferred income tax expense or benefit as the entity has incurred losses since inception and has provided a full valuation allowance against its deferred tax assets.

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

**(including data applicable to unaudited periods)
(Information as of June 30, 2017 and for the
six months ended June 30, 2016 and 2017 is unaudited)**

(In thousands, except share and per share information)

11. Income Tax (Continued)

A reconciliation of the income tax benefit at the federal statutory tax rate to the Company's effective income tax rate follows:

	Year Ended December 31,	
	2015	2016
Statutory tax rate	34.00%	34.00%
State tax, net of federal benefit	4.33%	2.63%
Research and development credit	0.85%	1.34%
Orphan drug credit	1.91%	2.15%
Non deductible deferred issuance costs	—%	(2.40)%
Other	(2.23)%	(1.32)%
Non deductible warrant expense	(2.82)%	—%
Change in valuation allowance	(36.04)%	(36.40)%
Effective tax rate	0.00%	0.00%

The principal components of the Company's deferred tax assets are as follows:

	As of December 31,	
	2015	2016
Deferred tax assets:		
Net operating loss carryforwards	\$ 9,481	\$ 17,248
Research and development credits	895	1,214
Orphan drug credit	322	1,164
Capitalized license fee	357	600
Other	16	262
Total gross deferred tax assets	11,071	20,488
Valuation allowance	(11,071)	(20,488)
Net deferred tax assets	\$ —	\$ —

ASC 740 requires a valuation allowance to reduce the deferred tax assets reported if, based on the weight of available evidence, it is more likely than not that some portion or all of the deferred tax assets will not be realized. After consideration of all the evidence, both positive and negative, the Company has recorded a full valuation allowance against its deferred tax assets at December 31, 2015 and 2016, because the Company's management has determined that it is more likely than not that these assets will not be realized. The increase in the valuation allowance of \$4,012 in 2015 and \$9,417 in 2016 primarily relates to the net loss incurred by the Company during each period.

As of December 31, 2016, the Company had federal and state net operating loss carryforwards of approximately \$46,934 and \$24,432, respectively, which are available to reduce future taxable income. The net operating loss carryforwards expire at various times beginning in 2033 for federal and state purposes.

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

**(including data applicable to unaudited periods)
(Information as of June 30, 2017 and for the
six months ended June 30, 2016 and 2017 is unaudited)**

(In thousands, except share and per share information)

11. Income Tax (Continued)

As of December 31, 2016, the Company had federal and state research tax credits of approximately \$971 and \$369, respectively, which may be used to offset future tax liabilities. Additionally, as of December 31, 2016, the Company had a federal orphan drug credit related to qualifying research of \$1,164. These tax credit carryforwards will begin to expire at various times beginning in 2033 for federal purposes and 2028 for state purposes.

The net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions and other provisions within the Internal Revenue Code. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years.

The Company has not recorded any reserves for uncertain tax positions as of December 31, 2015 and 2016 and June 30, 2017. The Company has not, as yet, conducted a study of research and development credit carryforwards. This study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the balance sheets or statements of operations and comprehensive loss if an adjustment were required.

Interest and penalty charges, if any, related to unrecognized tax benefits will be classified as income tax expense in the accompanying statements of operations and comprehensive loss. As of December 31, 2015 and 2016 and June 30, 2017, the Company had no accrued interest or penalties related to uncertain tax positions.

The Company is subject to examination by the U.S. federal, state and local income tax authorities for tax years 2013 forward. The Company is not currently under examination by the Internal Revenue Service or any other jurisdictions for any tax years.

12. Subsequent Events

The Company completed an evaluation of all subsequent events after the audited balance sheet date as of December 31, 2016 through May 23, 2017, the date the financial statements were issued and through September 22, 2017, the date the revised financial statements were available to be issued, to ensure that this filing includes appropriate disclosure of events both recognized in the financial statements as of December 31, 2016, and events which occurred subsequently but were not recognized in the financial statements.

Rhythm Pharmaceuticals, Inc.**Notes to Financial Statements (Continued)**

**(including data applicable to unaudited periods)
(Information as of June 30, 2017 and for the
six months ended June 30, 2016 and 2017 is unaudited)**

(In thousands, except share and per share information)

12. Subsequent Events (Continued)

The Company has completed an evaluation of all subsequent events after the unaudited balance sheet date of June 30, 2017 through August 23, 2017, the date the financial statements were issued and through September 22, 2017, the date the revised financial statements were available to be issued, to ensure that this filing includes appropriate disclosure of events both recognized in the financial statements as of June 30, 2017, and events which occurred subsequently, but were not recognized in the financial statements.

On August 18, 2017 the Series A Investors waived the \$5.0 million cash balance requirement of the Series A Investor Right/Obligation and closed on the second tranche of the January 2017 Series A Preferred Stock financing. The Company issued 20,474,998 shares of Series A Convertible Preferred Stock, par value \$0.001 per share, at a purchase price of \$1.00 per share, resulting in gross proceeds of \$20,475 to the Company.

On August 21, 2017, the LLC entity exchanged 8,578,646 of its shares of the Company's common stock for 78,666,209 shares of the Company's series A-1 junior preferred stock and the LLC entity distributed all of its shares of the Company's series A-1 junior preferred stock to the holders of its preferred units and the remaining 1,617,646 shares of its common stock to the holders of its common units. Following this Distribution, the LLC entity no longer owns any of the Company's shares. The series A-1 junior preferred stock is not redeemable and does not have a stated dividend or liquidation preference. These shares will convert to common stock on a 9.17-for-1 basis upon the earlier of (i) a qualified public offering with gross proceeds of at least \$50,000 and a price of not less than \$1.00 per share, subject to appropriate adjustment for any stock dividend, stock split, combination or other similar recapitalization, and (ii) the date specified by vote or written consent of the holders of the requisite holders of series A preferred stock and series A-1 preferred stock.

On August 21, 2017, the Company filed a third amended and restated certificate of incorporation with the Secretary of State of the State of Delaware to increase its authorized number of shares of common stock to 29,919,979 shares of common stock, \$0.001 par value per share.

13. Reverse Stock Split

On September 22, 2017, the Company's board of directors approved a 1-for-9.17 reverse stock split of the Company's issued and outstanding shares of common stock. All share and per share amounts in the financial statements and notes thereto have been retrospectively adjusted for all periods presented to give effect of the reverse stock split including reclassifying an amount equal to the reduction in par value of common stock to additional paid-in capital.

On September 22, 2017, the Company's board of directors approved an amended and restated certificate of incorporation to authorize 29,919,979 shares of common stock, \$0.001 par value per share and 159,616,209 shares of preferred stock, \$0.001 par value per share.

* * * * *

6,666,666 Shares



Common Stock

PRELIMINARY PROSPECTUS

MORGAN STANLEY

BofA MERRILL LYNCH

COWEN

NEEDHAM & COMPANY

Until _____, all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

, 2017

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution.

The following table sets forth the fees and expenses in connection with the issuance and distribution of the securities being registered (excluding the underwriting discount). Except for the SEC registration fee and the FINRA filing fee, all amounts are estimates.

	<u>Amount Paid or to be Paid</u>
SEC registration fee	\$ 13,328.50
FINRA filing fee	15,000
NASDAQ listing fee	125,000
Legal fees and expenses	1,500,000
Accounting fees and expenses	450,000
Printing expenses	250,000
Transfer and registrar fee	5,000
Miscellaneous	<u>41,671.50</u>
Total	<u>2,400,000</u>

Item 14. Indemnification of Directors and Officers.

Section 145 of the Delaware General Corporation Law authorizes a corporation's board of directors to grant, and authorizes a court to award, indemnity to officers, directors, and other corporate agents.

As permitted by Delaware law, our amended and restated certificate of incorporation provides that, to the fullest extent permitted by Delaware law, no director will be personally liable to us or our stockholders for monetary damages for breach of fiduciary duty as a director. Pursuant to Delaware law such protection would be not available for liability:

- for any breach of a duty of loyalty to us or our stockholders;
- for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- for any transaction from which the director derived an improper benefit; or
- for an act or omission for which the liability of a director is expressly provided by an applicable statute, including unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law.

Our amended and restated certificate of incorporation also provides that if Delaware law is amended after the approval by our stockholders of the amended and restated certificate of incorporation to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law.

Our amended and restated bylaws further provide that we must indemnify our directors and officers to the fullest extent permitted by Delaware law. Our amended and restated bylaws also authorize us to indemnify any of our employees or agents and permit us to secure insurance on behalf of any officer, director, employee or agent for any liability arising out of his or her action in that capacity, whether or not Delaware law would otherwise permit indemnification.

In addition, our amended and restated bylaws also provide that we are required to advance expenses to our directors and officers as incurred in connection with legal proceedings against them for which they may be indemnified and that the rights conferred in the amended and restated bylaws are not exclusive.

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We intend to enter into indemnification agreements with each of our directors and executive officers. These agreements, among other things, would require us to indemnify each director and officer to the fullest extent permitted by Delaware law, the amended and restated certificate of incorporation and amended and restated bylaws, for expenses such as, among other things, attorneys' fees, judgments, fines, and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action by or in our right, arising out of the person's services as our director or executive officer or as the director or executive officer of any subsidiary of ours or any other company or enterprise to which the person provides services at our request. Upon consummation of the offering, we intend to obtain and maintain directors' and officers' liability insurance.

The SEC has taken the position that personal liability of directors for violation of the federal securities laws cannot be limited and that indemnification by us for any such violation is unenforceable. The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against our directors and officers for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and other stockholders. Further, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement and damage awards against directors and officers as required by these indemnification provisions.

Item 15. Recent Sales of Unregistered Securities

Set forth below is information regarding securities we have issued within the past three years that were not registered under the Securities Act:

On August 3, 2015, December 1, 2015, January 6, 2017 and August 18, 2017 we issued 25,000,000 shares, 15,000,000, 20,475,001 and 20,474,998 shares, respectively, of series A preferred stock, \$0.001 par value per share, to a number of accredited investors for \$1.00 per share. These shares were issued in reliance on Regulation D, Rule 506 and/or Rule 4(2) under the Securities Act.

From January 1, 2014 through September 22, 2017, we granted options under the Plan to purchase an aggregate of 2,088,769 shares of our common stock to employees, consultants and directors, having exercise prices ranging from \$4.59 to \$8.44 per share. During this period, 152,671 of these stock options were exercised and 114,503 were forfeited.

The offers and sales of the securities described in the foregoing paragraph were exempt from registration under Rule 701 promulgated under the Securities Act in that the transactions were under compensatory benefit plans and contracts relating to compensation as provided under Rule 701. The recipients of such securities were our employees, directors or consultants and received the securities under the Plan. Appropriate legends were affixed to the securities issued in these transactions.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits

The exhibits to the registration statement are listed in the Exhibit Index attached hereto and incorporated by reference herein.

(b) Financial Statement Schedules

All financial statement schedules have been omitted because they are not required or because the required information is given in the financial statements or notes to those statements.

Item 17. Undertakings.

The undersigned Registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreement certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

The undersigned Registrant hereby undertakes that:

- (1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.
- (2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

EXHIBIT INDEX

Number	Description
1.1	<u>Form of Underwriting Agreement.</u>
3.1#	<u>Amended and Restated Certificate of Incorporation of the Registrant.</u>
3.2	<u>Bylaws of the Registrant.</u>
3.3	<u>Form of Amended and Restated Certificate of Incorporation of the Registrant to become effective upon the closing of this offering.</u>
3.4	<u>Form of Certificate of Amendment to Amended and Restated Certificate of Incorporation of the Registrant, effecting a stock split, to be in effect prior to the effectiveness of this registration statement.</u>
3.5	<u>Form of Amended and Restated Bylaws of the Registrant to become effective upon the closing of this offering.</u>
4.1	<u>Form of Common Stock Certificate of the Registrant.</u>
4.2#	<u>Amended and Restated Investors' Rights Agreement, dated August 21, 2017, by and among the Registrant and the investors set forth therein.</u>
5.1	<u>Opinion of Morgan, Lewis & Bockius LLP.</u>
10.1†	<u>Form of Indemnification Agreement by and between the Registrant and its directors and officers.</u>
10.2†	<u>2017 Equity Incentive Plan and Form of Option Agreement and Notice of Exercise.</u>
10.3†#	<u>Offer Letter, dated November 16, 2016, by and between the Registrant and Bart Henderson.</u>
10.4†#	<u>Offer Letter, dated November 16, 2016, by and between the Registrant and Keith M. Gottesdiener.</u>
10.5†#	<u>Offer Letter, dated November 16, 2016, by and between the Registrant and Fred T. Fiedorek.</u>
10.6‡#	<u>License Agreement, dated March 21, 2013, by and between the Registrant (f/k/a Rhythm Metabolic, Inc.) and Ipsen Pharma S.A.S.</u>
10.7‡#	<u>Development and Manufacturing Services Agreement, dated July 17, 2013, by and between the Registrant (f/k/a Rhythm Metabolic, Inc.) and Peptisyntha Inc. (n/k/a Corden Pharma International).</u>
10.8‡	<u>License Agreement dated January 4, 2016, by and between the Registrant and Camurus AB</u>
10.9#	<u>Amended and Restated Payroll Services Agreement, dated March 21, 2013, by and between the Registrant (f/k/a Rhythm Metabolic, Inc.) and Rhythm Pharmaceuticals, Inc.</u>
10.10†	<u>Rhythm Pharmaceuticals, Inc. 2017 Employee Stock Purchase Plan.</u>
10.11#	<u>Lease, dated November 25, 2015, by and between 500 Boylston & 222 Berkeley Owner (DE) LLC and the Registrant.</u>
10.12#	<u>Consulting Agreement, dated June 12, 2017, by and between the Registrant and Bart Henderson.</u>

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Number	Description
10.13†	Offer Letter, dated September 13, 2017, by and between the Registrant and Keith M. Gottesdiener.
10.14†	Offer Letter, dated September 13, 2017, by and between the Registrant and Fred T. Fiedorek.
10.15#	Development and Manufacturing Services Agreement, dated as of December 21, 2016, by and between Registrant and Recipharm Monts S.A.S.
10.16†#	Offer Letter, dated July 17, 2017, by and between the Registrant and Hunter Smith.
10.17†#	Offer Letter, dated July 5, 2017, by and between the Registrant and Nithya Desikan.
10.18†	Offer Letter, dated September 13, 2017, by and between the Registrant and Hunter Smith.
10.19†	Offer Letter, dated September 13, 2017, by and between the Registrant and Nithya Desikan.
10.20†#	Summary of Non-Employee Director Compensation Policy.
10.21†	2015 Equity Incentive Plan and Form of Option Agreement and Notice of Exercise.
23.1	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm.
23.2	Consent of Morgan, Lewis & Bockius LLP. Reference is made to Exhibit 5.1.
24.1#	Power of Attorney. Reference is made to the signature page hereto.

* To be filed by amendment.

Previously filed.

† Indicates management contract or compensatory plan.

‡ Indicates confidential treatment has been requested with respect to specific portions of this exhibit. Omitted portions have been filed with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the city of Boston, Commonwealth of Massachusetts on September 25, 2017.

RHYTHM PHARMACEUTICALS, INC.By: /s/ KEITH M. GOTTESDIENER

Keith M. Gottesdiener
Chief Executive Officer, President and Director

Pursuant to the requirements of the Securities Act, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Name</u>	<u>Title</u>	<u>Date</u>
<u>/s/ KEITH M. GOTTESDIENER</u> Keith M. Gottesdiener	Chief Executive Officer, President and Director (Principal Executive Officer)	September 25, 2017
<u>/s/ HUNTER SMITH</u> Hunter Smith	Chief Financial Officer and Treasurer (Principal Financial and Accounting Officer)	September 25, 2017
*	Controller	September 25, 2017
John J. Hulbert		
*	Director	September 25, 2017
Neil Exter		
*	Director	September 25, 2017
Todd Foley		
*	Director	September 25, 2017
Christophe R. Jean		
*	Director	September 25, 2017
Ed Mathers		

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<u>Name</u>	<u>Title</u>	<u>Date</u>
*		
Jonathan T. Silverstein	Director	September 25, 2017
*		
David W. J. McGirr	Director	September 25, 2017
*		
David P. Meeker	Director, Chairman of the Board	September 25, 2017
*By:	/s/ KEITH M. GOTTESDIENER	
Keith M. Gottesdiener <i>Attorney-in-Fact</i>		September 25, 2017

Shares**Rhythm Pharmaceuticals, Inc.**

Common Stock
(\$0.001 par value)

UNDERWRITING AGREEMENT

, 2017

, 2017

Morgan Stanley & Co. LLC
Merrill Lynch, Pierce, Fenner & Smith
Incorporated
Cowen and Company, LLC
c/o Morgan Stanley & Co. LLC
1585 Broadway
New York, New York 10036

Ladies and Gentlemen:

Rhythm Pharmaceuticals, Inc., a Delaware corporation (the “**Company**”), proposes to issue and sell to the several Underwriters named in Schedule I hereto (the “**Underwriters**”), for whom you (the “**Representatives**”) are acting as representatives, shares of its common stock, \$0.001 par value per share (the “**Firm Shares**”). The Company also proposes to issue and sell to the several Underwriters not more than an additional shares of its common stock, \$0.001 par value per share (the “**Additional Shares**”) if and to the extent that you, as Managers of the offering, shall have determined to exercise, on behalf of the Underwriters, the right to purchase such shares of common stock granted to the Underwriters in Section 2 hereof. The Firm Shares and the Additional Shares are hereinafter collectively referred to as the “**Shares**.” The shares of common stock, \$0.001 par value per share, of the Company to be outstanding after giving effect to the sales contemplated hereby are hereinafter referred to as the “**Common Stock**.”

The Company has filed with the Securities and Exchange Commission (the “**Commission**”) a registration statement, including a prospectus, relating to the Shares. The registration statement as amended at the time it becomes effective, including the information (if any) deemed to be part of the registration statement at the time of effectiveness pursuant to Rule 430A under the Securities Act of 1933, as amended (the “**Securities Act**”), is hereinafter referred to as the “**Registration Statement**"; the prospectus in the form first used to confirm sales of Shares (or in the form first made available to the Underwriters by the Company to meet requests of purchasers pursuant to Rule 173 under the Securities Act) is hereinafter referred to as the “**Prospectus**.“ If the Company has filed an abbreviated registration statement to register additional shares of Common Stock pursuant to Rule 462(b) under the Securities Act (the “**Rule 462 Registration Statement**”), then any reference herein to the term “**Registration Statement**” shall be deemed to include such Rule 462 Registration Statement.

For purposes of this Agreement, “**free writing prospectus**” has the meaning set forth in Rule 405 under the Securities Act, “**Time of Sale Prospectus**” means the preliminary prospectus together with the documents and pricing information set forth in Schedule II hereto, and “**broadly available road show**” means a “bona fide electronic road show” as defined in Rule 433(h)(5) under the Securities Act that has been made

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available without restriction to any person. As used herein, the terms “Registration Statement,” “preliminary prospectus,” “Time of Sale Prospectus” and “Prospectus” shall include the documents, if any, incorporated by reference therein as of the date hereof.

As described in the Prospectus, in connection with the offering contemplated by this Agreement, on August 21, 2017, the Company exchanged (the “**Exchange**”) 78,666,209 shares of common stock of the Company for an equal-number of newly-issued shares of its Series A-1 Junior Preferred Stock, \$0.001 par value per share, (the “**Series A-1 Preferred Stock**”) with Rhythm Holding Company, LLC, a Delaware limited liability company (the “**Parent Entity**”). On August 21, 2017, the Parent Entity distributed all of its shares of Series A-1 Preferred Stock to holders of the Parent Entity’s preferred units and 14,833,791 shares of Common Stock of the Company to holders of the Parent Entity’s common units (the “**Distribution**”). In connection with the Exchange and the Distribution, the Company entered into that certain Exchange Agreement, that certain Amended and Restated Investors’ Rights Agreement, that certain Amended and Restated Right of First Refusal and Co-Sale Agreement, that certain Amended and Restated Voting Agreement and those certain Stock Restriction Agreements, in each case dated as of August 21, 2017, by and among the Company, the Parent Entity and the investors party thereto, (collectively, the “**Exchange and Distribution Documents**”)

1. *Representations and Warranties.* The Company represents and warrants to and agrees with each of the Underwriters that:

(a) The Registration Statement has become effective; no stop order suspending the effectiveness of the Registration Statement is in effect, and no proceedings for such purpose are pending before or threatened by the Commission.

(b) (i) The Registration Statement, when it became effective, did not contain and, as amended or supplemented, if applicable, will not contain any untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading, (ii) the Registration Statement and the Prospectus comply and, as amended or supplemented, if applicable, will comply in all material respects with the Securities Act and the applicable rules and regulations of the Commission thereunder, (iii) the Time of Sale Prospectus does not, and at the time of each sale

of the Shares in connection with the offering when the Prospectus is not yet available to prospective purchasers and at the Closing Date (as defined in Section 4), the Time of Sale Prospectus, as then amended or supplemented by the Company, if applicable, will not, contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading, (iv) each broadly available road show, if any, when considered together with the Time of Sale Prospectus, does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading and (v) the Prospectus does not contain and, as amended or supplemented, if applicable, will not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading, except that the representations and

warranties set forth in this paragraph do not apply to statements or omissions in the Registration Statement, the Time of Sale Prospectus or the Prospectus based upon information relating to any Underwriter furnished to the Company in writing by such Underwriter through you expressly for use therein.

(c) The Company is not an “ineligible issuer” in connection with the offering pursuant to Rules 164, 405 and 433 under the Securities Act. Any free writing prospectus that the Company is required to file pursuant to Rule 433(d) under the Securities Act has been, or will be, filed with the Commission in accordance with the requirements of the Securities Act and the applicable rules and regulations of the Commission thereunder. Each free writing prospectus that the Company has filed, or is required to file, pursuant to Rule 433(d) under the Securities Act or that was prepared by or on behalf of or used or referred to by the Company complies or will comply in all material respects with the requirements of the Securities Act and the applicable rules and regulations of the Commission thereunder. Except for the free writing prospectuses, if any, identified in Schedule II hereto, and electronic road shows, if any, each furnished to you before first use, the Company has not prepared, used or referred to, and will not, without your prior consent, prepare, use or refer to, any free writing prospectus.

(d) From the time of initial confidential submission of the Registration Statement to the Commission (or, if earlier, the first date on which the Company engaged directly or through any person authorized to act on its behalf in any Testing-the-Waters Communication) through the date hereof, the Company has been and is an “emerging growth company,” as defined in Section 2(a) of the Securities Act (an “**Emerging Growth Company**”). “**Testing-the-Waters Communication**” means any oral or written communication with potential investors undertaken in reliance on Section 5(d) of the Securities Act.

(e) The Company (i) has not alone engaged in any Testing-the-Waters Communication (other than Testing-the-Waters Communications with the consent of the Representatives with entities that are qualified institutional buyers within the meaning of Rule 144A under the Securities Act or institutions that are accredited investors within the meaning of Rule 501 under the Securities Act) and (ii) has not authorized anyone other than the Representatives to engage in Testing-the-Waters Communications. The Company reconfirms that the Representatives have been authorized to act on its behalf in undertaking Testing-the-Waters Communications. The Company has not distributed any Written Testing-the-Waters Communications other than those listed on Schedule III hereto. “**Written Testing-the-Waters Communication**” means any Testing-the-Waters Communication that is a written communication within the meaning of Rule 405 under the Securities Act.

(f) As of the time of each sale of the Shares in connection with the offering when the Prospectus is not yet available to prospective purchasers, none of (A) the Time of Sale Prospectus, (B) any free writing prospectus, when considered together with the Time of Sale Prospectus, and (C) any individual Written Testing-the-Waters Communication, when considered together with the Time of Sale Prospectus, included, includes or will include an untrue statement of a material fact or omitted, omits or will

omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading.

(g) The Company has been duly incorporated and is validly existing as a corporation in good standing under the laws of the jurisdiction in which it is chartered or organized with full corporate power and authority to own or lease, as the case may be, and to operate its properties and conduct its business as described in the Prospectus, any free writing prospectus and the Time of Sale Prospectus, and is duly qualified to do business as a foreign corporation and is in good standing under the laws of each jurisdiction which requires such qualification, except where the failure to be so qualified or in good standing would not reasonably be expected, individually or in the aggregate, to have a material adverse effect on the condition (financial or otherwise), prospects, earnings, business or properties of the Company taken as a whole, whether or not arising from transactions in the ordinary course of business (a “**Material Adverse Effect**”).

(h) The outstanding shares of capital stock of the Company have been duly and validly authorized and issued and are fully paid and nonassessable; the Shares have been duly and validly authorized and, when issued and delivered to and paid for by the Underwriters pursuant to this Agreement, will be fully paid and nonassessable; the holders of shares of capital stock of the Company are not entitled to preemptive or other rights to subscribe for the Shares; and, except as set forth in the Prospectus, any free writing prospectus and the Time of Sale Prospectus, no options, warrants or other rights to purchase, agreements or other obligations to issue, or rights to convert any obligations into or exchange any securities for, shares of capital stock of or ownership interests in the Company are outstanding. The authorized capital stock of the Company conforms as to legal matters to the description thereof contained in each of the Time of Sale Prospectus and the Prospectus.

(i) The Company does not currently own or control, directly or indirectly, any interest in any other corporation, partnership, trust, joint venture, limited liability company, association, or other business entity. The Company is not a participant in any joint venture, partnership or similar arrangement. For the avoidance of doubt, the Company has no subsidiaries.

(j) There is no contract or other document of a character required to be described in the Registration Statement or Time of Sale Prospectus, or to be filed as an exhibit thereto, which is not described or filed as required (and the Preliminary Prospectus contains in all material respects the same description of the foregoing matters contained in the Time of Sale Prospectus); and the statements in the Prospectus and the Time of Sale Prospectus under the headings “Material United States Federal Income and Estate Tax Consequences to Non-U.S. Holders of Our Common Stock,” “Risk Factors—Risks Related to Our Intellectual Property Rights,” “Risk Factors—Risks Related To Regulatory Approval and Marketing of Setmelanotide and Other Legal Compliance Matters,” “Business—Patents and Proprietary Rights”, and “Business—Regulatory Matters,” insofar as such statements summarize legal matters, agreements, documents or proceedings discussed therein, are accurate and fair summaries of such legal matters, agreements, documents or proceedings.

(k) This Agreement has been duly authorized, executed and delivered by the Company.

(l) There has not occurred any material adverse change, or any development involving a prospective material adverse change, in the condition, financial or otherwise, or in the earnings, business or operations of the Company from that set forth in the Time of Sale Prospectus.

(m) The Company is not and, after giving effect to the offering and sale of the Shares and the application of the proceeds thereof as described in the Prospectus, any free writing prospectus and the Time of Sale Prospectus, will not be an “investment company” as defined in the Investment Company Act of 1940, as amended.

(n) No consent, approval, authorization, filing with or order of any court or governmental agency or body is required in connection with the transactions contemplated herein, except such as have been obtained under the Securities Act and such as may be required under the blue sky laws of any jurisdiction in connection with the purchase and distribution of the Shares by the Underwriters in the manner contemplated herein and in the Prospectus, any free writing prospectus and the Time of Sale Prospectus.

(o) No consent, approval, authorization, filing with or order of any court or governmental agency or body was required in connection with the Exchange and Distribution Documents or the transactions contemplated thereby, except such as have been obtained or waived. The Exchange and Distribution Documents and the transactions contemplated thereby did not conflict with, result in a breach or violation of, or imposition of any lien, charge or encumbrance upon any property or assets of the Company pursuant to the charter or by-laws of the Company as in effect immediately prior to the Exchange and Distribution and do not conflict with, result in a breach or violation of, or imposition of any lien, charge or encumbrance upon any property or assets of the Company pursuant to (i) the charter or by-laws of the Company as in effect on the date hereof, (ii) the operating agreement of the Parent Entity, (iii) the terms of any indenture, contract, lease, mortgage, deed of trust, note agreement, loan agreement or other agreement, obligation, condition, covenant or instrument to which the Company is a party or bound or to which its property is subject, or (iv) any statute, law, rule, regulation, judgment, order or decree applicable to the Company, the Parent Entity or any of its subsidiaries of any court, regulatory body, administrative agency, governmental body, arbitrator or other authority having jurisdiction over the Company, the Parent Entity or any of its subsidiaries or any of its or their properties, except in the case of clauses (iii) and (iv) as would not reasonably be expected to, either individually or in the aggregate, result in a Material Adverse Effect.

(p) Neither the issue and sale of the Shares nor the consummation of any other of the transactions herein contemplated nor the fulfillment of the terms hereof will conflict with, result in a breach or violation of, or imposition of any lien, charge or encumbrance upon any property or assets of the Company pursuant to, (i) the charter or by-laws of the Company, (ii) the terms of any indenture, contract, lease, mortgage, deed

of trust, note agreement, loan agreement or other agreement, obligation, condition, covenant or instrument to which the Company is a party or bound or to which its property is subject, or (iii) any statute, law, rule, regulation, judgment, order or decree applicable to the Company of any court, regulatory body, administrative agency, governmental body, arbitrator or other authority having jurisdiction over the Company or any of its properties, except in the case of clauses (ii) and (iii) as would not have a Material Adverse Effect.

(q) No holders of securities of the Company have rights to the registration of such securities under the Registration Statement, except such rights which have been duly waived in accordance with their terms and with the General Corporation Law of the State of Delaware.

(r) The consolidated historical financial statements and schedules of the Company included in the Prospectus, the Time of Sale Prospectus and the Registration Statement present fairly in all material respects the financial condition, results of operations and cash flows of the Company as of the dates and for the periods indicated, comply as to form in all material respects with the applicable accounting requirements of the Securities Act and have been prepared in conformity with generally accepted accounting principles applied on a consistent basis throughout the periods involved (except as otherwise noted therein). The selected financial data set forth under the caption “Selected Financial Information” in the Prospectus, the Time of Sale Prospectus and Registration Statement fairly present, on the basis stated in the Prospectus, the Time of Sale Prospectus and the Registration Statement, the information included therein. The pro forma financial statements included in the Prospectus, the Time of Sale Prospectus and the Registration Statement include assumptions that provide a reasonable basis for presenting the significant effects directly attributable to the transactions and events described therein, the related pro forma adjustments give appropriate effect to those assumptions, and the pro forma adjustments reflect the proper application of those adjustments to the historical financial statement amounts in the pro forma financial statements included in the Prospectus, the Time of Sale Prospectus and the Registration Statement. The pro forma financial statements included in the Prospectus, the Time of Sale Prospectus and the Registration Statement comply as to form in all material respects with the applicable accounting requirements of Regulation S-X under the Securities Act and the pro forma adjustments have been properly applied to the historical amounts in the compilation of those statements.

(s) No action, suit or proceeding by or before any court or governmental agency, authority or body or any arbitrator involving the Company or its property is pending or, to the knowledge of the Company, threatened that could reasonably be expected to have a Material Adverse Effect, except as set forth in or contemplated in the Prospectus, any free writing prospectus and the Time of Sale Prospectus (exclusive of any supplement thereto).

(t) The Company owns or leases all such properties as are necessary to the conduct of its operations as presently conducted in all material respects.

(u) The Company is not in violation or default of (i) its charter or bylaws, (ii) the terms of any indenture, contract, lease, mortgage, deed of trust, note agreement, loan agreement or other agreement, obligation, condition, covenant or instrument to which it is a party or bound or to which its property is subject, or (iii) any statute, law, rule, regulation, judgment, order or decree of any court, regulatory body, administrative agency, governmental body,

arbitrator or other authority having jurisdiction over the Company or any of its properties, as applicable, except in the case of clauses (ii) and (iii), for such breach or violation as would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect.

(v) Ernst & Young LLP, who have certified certain financial statements of the Company and delivered their report with respect to the audited financial statements and schedules included in the Prospectus, any free writing prospectus and the Time of Sale Prospectus, are independent public accountants with respect to the Company within the meaning of the Securities Act and the applicable published rules and regulations thereunder.

(w) There are no transfer taxes or other similar fees or charges under Federal law or the laws of any state, or any political subdivision thereof, required to be paid in connection with the execution and delivery of this Agreement or the issuance by the Company or sale by the Company of the Shares.

(x) The Company has filed all tax returns that are required to be filed or has requested extensions thereof (except in any case in which the failure so to file would not have a Material Adverse Effect, except as set forth in or contemplated in the Prospectus, any free writing prospectus and the Time of Sale Prospectus (exclusive of any supplement thereto)) and has paid all taxes required to be paid by it and any other assessment, fine or penalty levied against it, to the extent that any of the foregoing is due and payable, except for any such assessment, fine or penalty that is currently being contested in good faith or as would not have a Material Adverse Effect.

(y) No labor problem or dispute with the employees of the Company exists or, to the knowledge of the Company, is threatened or imminent, and the Company is not aware of any existing or imminent labor disturbance by the employees of any of its principal suppliers, contractors or customers, that could have a Material Adverse Effect.

(z) The Company is insured by insurers of recognized financial responsibility against such losses and risks and in such amounts as the Company reasonably believes are prudent and customary in the businesses in which it is engaged; all policies of insurance and fidelity or surety bonds insuring the Company or its business, assets, employees, officers and directors are in full force and effect; the Company is in compliance with the terms of such policies and instruments in all material respects; and there are no claims by the Company under any such policy or instrument as to which any insurance company is denying liability or defending under a reservation of rights clause; the Company has not been refused any insurance coverage sought or applied for; and the Company has no reason to believe that it will not be able to renew its existing insurance coverage as and when such coverage expires or to obtain similar coverage from similar

insurers as may be necessary to continue its business at a cost that would not have a Material Adverse Effect.

(aa) The Company possesses all licenses, certificates, permits and other authorizations issued by all applicable authorities necessary to conduct its business, except in each case, the lack of which would not reasonably be expected, individually or in the aggregate, to have a Material Adverse Effect, and the Company has not received any notice of proceedings relating to the revocation or modification of any such certificate, authorization or permit which, singly or in the aggregate, if the subject of an unfavorable decision, ruling or finding, would have a Material Adverse Effect.

(bb) The Company maintains a system of internal accounting controls sufficient to provide reasonable assurance that (i) transactions are executed in accordance with management's general or specific authorizations; (ii) transactions are recorded as necessary to permit preparation of financial statements in conformity with generally accepted accounting principles and to maintain asset accountability; (iii) access to assets is permitted only in accordance with management's general or specific authorization; and (iv) the recorded accountability for assets is compared with the existing assets at reasonable intervals and appropriate action is taken with respect to any differences. The Company's internal controls over financial reporting are effective and the Company is not aware of any material weakness in its internal controls over financial reporting.

(cc) The Company maintains "disclosure controls and procedures" (as such term is defined in Rule 13a-15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act")); such disclosure controls and procedures are effective.

(dd) The Company has not taken, directly or indirectly, without giving effect to any activities of the Underwriters, any action designed to or that would constitute or that might reasonably be expected to cause or result in, under the Exchange Act or otherwise, stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of the Shares.

(ee) Except in each case as would not reasonably be expected, individually or in the aggregate, to have a Material Adverse Effect, the Company (i) is in compliance with any and all applicable foreign, federal, state and local laws and regulations relating to the protection of human health and safety, the environment or hazardous or toxic substances or wastes, pollutants or contaminants ("Environmental Laws"), (ii) has received and is in compliance with all permits, licenses or other approvals required of it under applicable Environmental Laws to conduct its business and (iii) has not received notice of any actual or potential liability under any environmental law. The Company has not been named as a "potentially responsible party" under the Comprehensive Environmental Response, Compensation, and Liability Act of 1980, as amended.

(ff) None of the following events has occurred or exists: (i) a failure to fulfill the obligations, if any, under the minimum funding standards of Section 302 of the United States Employee Retirement Income Security Act of 1974, as amended ("ERISA"), and the regulations and published interpretations thereunder with respect to a

Plan that is required to be funded, determined without regard to any waiver of such obligations or extension of any amortization period that would reasonably be expected to have a Material Adverse Effect; (ii) an audit or investigation by the Internal Revenue Service, the U.S. Department of Labor, the Pension Benefit Guaranty Corporation or any other federal or state governmental agency or any foreign regulatory agency with respect to the employment or compensation of employees by the Company that would reasonably be expected to have a Material Adverse Effect; (iii) any breach of any contractual obligation, or any violation of law or applicable qualification standards, with respect to the employment or compensation of employees by the Company that would reasonably be expected to have a Material Adverse Effect. None of the following events has occurred or is reasonably likely to occur: (i) a material increase in the aggregate amount of contributions required to be made to all Plans in the current fiscal year of the Company compared to the amount of such contributions made in the most recently completed fiscal year of the Company; (ii) a material increase in the "accumulated post-retirement benefit

obligations” (within the meaning of Statement of Financial Accounting Standards 106) of the Company compared to the amount of such obligations in the most recently completed fiscal year of the Company; (iii) any event or condition giving rise to a liability under Title IV of ERISA that would reasonably be expected to have a Material Adverse Effect; or (iv) the filing of a claim by one or more employees or former employees of the Company related to their employment that would reasonably be expected to have a Material Adverse Effect. For purposes of this paragraph, the term “Plan” means a plan (within the meaning of Section 3(3) of ERISA) subject to Title IV of ERISA with respect to which the Company may have any liability.

(gg) There is and has been no failure on the part of the Company and any of the Company’s directors or officers, in their capacities as such, to comply with any provision of the Sarbanes-Oxley Act of 2002 and the rules and regulations promulgated in connection therewith (the “**Sarbanes-Oxley Act**”), including Section 402 relating to loans.

(hh) (i) None of the Company, or any director, officer, or employee thereof, or, to the Company’s knowledge, any agent or representative of the Company, has taken or will take any action in furtherance of an offer, payment, promise to pay, or authorization or approval of the payment, giving or receipt of money, property, gifts or anything else of value, directly or indirectly, to any government official (including any officer or employee of a government or government-owned or controlled entity or of a public international organization, or any person acting in an official capacity for or on behalf of any of the foregoing, or any political party or party official or candidate for political office) in order to influence official action, or to any person in violation of any applicable anti-corruption laws; (ii) the Company has conducted its business in compliance with applicable anti-corruption laws and has instituted and maintained and will continue to maintain policies and procedures reasonably designed to promote and achieve compliance with such laws and with the representations and warranties contained herein; and (iii) the Company will not use, directly or indirectly, the proceeds of the offering in furtherance of an offer, payment, promise to pay, or authorization of the payment or giving of money, or anything else of value, to any person in violation of any applicable anti-corruption laws.

(ii) The operations of the Company are and have been conducted at all times in material compliance with all applicable financial recordkeeping and reporting requirements, including those of the Bank Secrecy Act, as amended by Title III of the Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act of 2001 (USA PATRIOT Act), and the applicable anti-money laundering statutes of jurisdictions where the Company conducts business, the rules and regulations thereunder and any related or similar rules, regulations or guidelines, issued, administered or enforced by any governmental agency (collectively, the “**Anti-Money Laundering Laws**”), and no action, suit or proceeding by or before any court or governmental agency, authority or body or any arbitrator involving the Company with respect to the Anti-Money Laundering Laws is pending or, to the best knowledge of the Company, threatened.

(jj) (i) None of the Company, or any director, officer, or employee thereof, or, to the Company’s knowledge, any agent, affiliate or representative of the Company, is an individual or entity (“**Person**”) that is, or is owned or controlled by one or more Persons that are

(A) the subject of any sanctions administered or enforced by the U.S. Department of Treasury’s Office of Foreign Assets Control (“**OFAC**”), the United Nations Security Council (“**UNSC**”), the European Union (“**EU**”), Her Majesty’s Treasury (“**HMT**”), or other relevant sanctions authority (collectively, “**Sanctions**”), or

(B) located, organized or resident in a country or territory that is the subject of Sanctions (including, without limitation, Crimea, Cuba, Iran, North Korea, Sudan and Syria).

(ii) The Company will not, directly or indirectly, use the proceeds of the offering, or lend, contribute or otherwise make available such proceeds to any joint venture partner or other Person:

(A) to fund or facilitate any activities or business of or with any Person or in any country or territory that, at the time of such funding or facilitation, is the subject of Sanctions; or

(B) in any other manner that will result in a violation of Sanctions by any Person (including any Person participating in the offering, whether as underwriter, advisor, investor or otherwise).

(iii) For the past 5 years, the Company has not knowingly engaged in, is not now knowingly engaged in, and will not engage in, any dealings or transactions with any Person, or in any country or territory, that at the time of the dealing or transaction is or was the subject of Sanctions.

(kk) The Company owns, possesses, licenses or has other rights to use, on reasonable terms, all patents, patent applications, trade and service marks, trade and service mark registrations, trade names, copyrights, licenses, inventions, trade secrets,

technology, know-how and other intellectual property (collectively, the “**Intellectual Property**”) necessary for the conduct of the Company’s business in all material respects as now conducted or as proposed in the Prospectus to be conducted. Except as set forth in the Prospectus, any free writing prospectus and the Time of Sale Prospectus under the captions “Risk Factors—Risks Related to Our Intellectual Property Rights” and “Business—Patents and Proprietary Rights,” (a) there are no rights of third parties to any such Intellectual Property; (b) to the Company’s knowledge, there is no material infringement by third parties of any such Intellectual Property; (c) there is no pending or, to the Company’s knowledge, threatened action, suit, proceeding or claim by others challenging the Company’s rights in or to any such Intellectual Property, and, except as would not reasonably be expected to have a Material Adverse Effect, the Company is unaware of any facts which would form a reasonable basis for any such claim; (d) there is no pending or, to the Company’s knowledge, threatened action, suit, proceeding or claim by others challenging the validity or scope of any such Intellectual Property, and, except as would not reasonably be expected to have a Material Adverse Effect, the Company is unaware of any facts which would form a reasonable basis for any such claim; (e) there is no pending or, to the Company’s knowledge, threatened action, suit, proceeding or claim by others that the Company infringes or otherwise violates any patent, trademark, copyright, trade secret or other proprietary rights of others, and, except as would not reasonably be expected to have a Material Adverse Effect, the Company is unaware of any other fact which would form a reasonable basis for any such claim; (f) there is no U.S. patent which contains claims that dominate any Intellectual Property described in the Prospectus, any free writing prospectus and the Time of Sale Prospectus as being owned by or licensed to the Company or that interferes with the issued claims of any such Intellectual Property; and (g) there is no prior art that may render any U.S. patent held by

the Company invalid, and all prior art of which the Company is aware that may be material to the validity of a U.S. patent or to the patentability of a U.S. patent application has been disclosed to the U.S. Patent and Trademark Office.

(ll) The statements contained in the Prospectus and the Time of Sale Prospectus under the captions “Risk Factors — Risks Related to Our Intellectual Property Rights” and “Business — Patents and Proprietary Information,” insofar as such statements summarize legal matters, agreements, documents, or proceedings discussed therein, are accurate and fair summaries of such legal matters, agreements, documents or proceedings.

(mm) Except as described in the Registration Statement, the Prospectus, any free writing prospectus and the Time of Sale Prospectus, as applicable, the Company (i) is and at all times has been in compliance with all local, state, federal, national, supranational and foreign statutes, rules and regulations applicable to the ownership, testing, development, manufacture, packaging, processing, use, storage, import, export or disposal of any product manufactured or distributed by the Company, including, without limitation, the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 301 et seq.), and the federal Anti-kickback Statute (42 U.S.C. § 1320a-7b(b)), the regulations promulgated pursuant to such laws, and any successor government programs, and comparable state laws, regulations relating to Good Laboratory Practices and Good Clinical Practices (collectively, the “**Applicable Laws**”), except for such non-compliance as would not,

individually or in the aggregate, have a Material Adverse Effect; (ii) has not received any notice from any court or arbitrator or governmental or regulatory authority alleging or asserting non-compliance with any Applicable Laws or any licenses, exemptions, certificates, approvals, clearances, authorizations, permits, registrations and supplements or amendments thereto required by any such Applicable Laws (“**Authorizations**”), except for such non- compliance as would not, individually or in the aggregate, have a Material Adverse Effect; (iii) possesses all material Authorizations and such Authorizations are valid and in full force and effect and is not in violation of any term of any such Authorizations, except for such violations as would not, individually or in the aggregate, have a Material Adverse Effect; (iv) has not received written notice of any claim, action, suit, proceeding, hearing, enforcement, investigation, arbitration or other action from any court or arbitrator or governmental or regulatory authority alleging that any product operation or activity is in violation of any Applicable Laws or Authorizations nor, to the Company’s knowledge, is any such claim, action, suit, proceeding, hearing, enforcement, investigation, arbitration or other action threatened, except such as would not, individually or in the aggregate, have a Material Adverse Effect; (v) has not received written notice that any court or arbitrator or governmental or regulatory authority has taken, is taking or intends to take action to materially limit, suspend, materially modify or revoke any Authorizations nor, to the Company’s knowledge, is any such limitation, suspension, modification or revocation threatened, except such as would not, individually or in the aggregate, have a Material Adverse Effect; (vi) has filed, obtained, maintained or submitted all material reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments as required by any Applicable Laws or Authorizations and that all such reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments were complete and accurate on the date filed in all material respects (or were corrected or supplemented by a subsequent submission); and (vii) is not a party to any corporate integrity agreements, monitoring agreements, consent decrees, settlement orders, or similar agreements with or imposed by any governmental or regulatory authority.

(nn) Subsequent to the respective dates as of which information is given in each of the Registration Statement, the Time of Sale Prospectus and the Prospectus, (i) the Company has not incurred any material liability or obligation, direct or contingent, nor entered into any material transaction; (ii) the Company has not purchased any of its outstanding capital stock, nor declared, paid or otherwise made any dividend or distribution of any kind on its capital stock other than ordinary and customary dividends; and (iii) there has not been any material change in the capital stock, short-term debt or long-term debt of the Company, except in each case as described in each of the Registration Statement, the Time of Sale Prospectus and the Prospectus, respectively.

(oo) Except as described in the Time of Sale Prospectus, the Company has not sold, issued or distributed any shares of Common Stock during the six-month period preceding the date hereof, including any sales pursuant to Rule 144A under, or Regulation D or S of, the Securities Act, other than shares issued pursuant to employee benefit plans, qualified stock option plans or other employee compensation plans or pursuant to outstanding options, rights or warrants.

(pp) Any certificate signed by any officer of the Company and delivered to the Representatives or counsel for the Underwriters in connection with the offering of the Shares shall be deemed a representation and warranty by the Company, as to matters covered thereby, to each Underwriter.

2. *Agreements to Sell and Purchase.* The Company hereby agrees to sell to the several Underwriters, and each Underwriter, upon the basis of the representations and warranties herein contained, but subject to the conditions hereinafter stated, agrees, severally and not jointly, to purchase from the Company the respective numbers of Firm Shares set forth in Schedule I hereto opposite its name at \$[] a share (the “**Purchase Price**”).

On the basis of the representations and warranties contained in this Agreement, and subject to its terms and conditions, the Company agrees to sell to the Underwriters the Additional Shares, and the Underwriters shall have the right to purchase, severally and not jointly, up to [] Additional Shares at the Purchase Price, provided, however, that the amount paid by the Underwriters for any Additional Shares shall be reduced by an amount per share equal to any dividends declared by the Company and payable on the Firm Shares but not payable on such Additional Shares. You may exercise this right on behalf of the Underwriters in whole or from time to time in part by giving written notice not later than 30 days after the date of this Agreement. Any exercise notice shall specify the number of Additional Shares to be purchased by the Underwriters and the date on which such shares are to be purchased. Each purchase date must be at least one business day after the written notice is given and may not be earlier than the closing date for the Firm Shares nor later than ten business days after the date of such notice. Additional Shares may be purchased as provided in Section 4 hereof solely for the purpose of covering sales of shares in excess of the number of the Firm Shares. On each day, if any, that Additional Shares are to be purchased (an “**Option Closing Date**”), each Underwriter agrees, severally and not jointly, to purchase the number of Additional Shares (subject to such adjustments to eliminate fractional shares as you may determine) that bears the same proportion to the total number of Additional Shares to be purchased on such Option Closing Date as the number of Firm Shares set forth in Schedule I hereto opposite the name of such Underwriter bears to the total number of Firm Shares.

3. *Terms of Public Offering.* The Company is advised by you that the Underwriters propose to make a public offering of their respective portions of the Shares as soon after the Registration Statement and this Agreement have become effective as in your judgment is advisable. The Company is further advised by you that the Shares are to be offered to the public initially at \$[] a share (the “**Public Offering Price**”) and to certain dealers selected by you at a price that represents a concession not in excess of \$[] a share under the Public Offering Price, and that any Underwriter may allow, and such dealers may reallow, a concession, not in excess of \$[] a share, to any Underwriter or to certain other dealers.

4. *Payment and Delivery.* Payment for the Firm Shares shall be made to the Company in Federal or other funds immediately available in New York City against

delivery of such Firm Shares for the respective accounts of the several Underwriters at 10:00 a.m., New York City time, on _____, 2017, or at such other time on the same or such other date, not later than _____, 2017, as shall be designated in writing by you. The time and date of such payment are hereinafter referred to as the “**Closing Date**.”

Payment for any Additional Shares shall be made to the Company in Federal or other funds immediately available in New York City against delivery of such Additional Shares for the respective accounts of the several Underwriters at 10:00 a.m., New York City time, on the date specified in the corresponding notice described in Section 2 or at such other time on the same or on such other date, in any event not later than _____, 2017, as shall be designated in writing by you.

The Firm Shares and Additional Shares shall be registered in such names and in such denominations as you shall request in writing not later than one full business day prior to the Closing Date or the applicable Option Closing Date, as the case may be. The Firm Shares and Additional Shares shall be delivered to you on the Closing Date or an Option Closing Date, as the case may be, for the respective accounts of the several Underwriters, with any transfer taxes payable in connection with the transfer of the Shares to the Underwriters duly paid, against payment of the Purchase Price therefor.

5. *Conditions to the Underwriters’ Obligations.* The obligations of the several Underwriters hereunder are subject to the accuracy of the representations and warranties of the Company contained herein or in certificates of any officer of the Company delivered pursuant to the provisions hereof, to the performance by the Company of its covenants and other obligations hereunder, and to the following further conditions:

(a) Subsequent to the execution and delivery of this Agreement and prior to the Closing Date:

- (i) there shall not have occurred any downgrading, nor shall any notice have been given of any intended or potential downgrading or of any review for a possible change that does not indicate the direction of the possible change, in the rating accorded any of the securities of the Company by any “nationally recognized statistical rating organization,” as such term is defined in Section 3(a)(62) of the Exchange Act; and
- (ii) there shall not have occurred any change, or any development involving a prospective change, in the condition, financial or

otherwise, or in the earnings, business or operations of the Company, taken as a whole, from that set forth in the Time of Sale Prospectus that, in your judgment, is material and adverse and that makes it, in your judgment, impracticable to market the Shares on the terms and in the manner contemplated in the Time of Sale Prospectus.

(b) The Underwriters shall have received on the Closing Date a certificate, dated the Closing Date and signed by an executive officer of the Company, to the effect set forth in Section 5(a)(i) above and to the effect that the representations and warranties of the Company contained in this Agreement are true and correct as of the Closing Date and that the Company has complied with all of the agreements and satisfied all of the conditions on its part to be performed or satisfied hereunder on or before the Closing Date.

The officer signing and delivering such certificate may rely upon the best of his or her knowledge as to proceedings threatened.

(c) The Underwriters shall have received on the Closing Date an opinion of Morgan, Lewis & Bockius LLP, outside counsel for the Company, substantially in the form attached hereto as Exhibit A-1.

(d) The Underwriters shall have received on the Closing Date opinions of Hogan Lovells LLP and Hogan Lovells International LLP, special regulatory counsel for the Company, each substantially in the form attached hereto as Exhibit A-2.

(e) The Underwriters shall have received on the Closing Date an opinion of Kendall Square IP Strategies, LLC, special intellectual property counsel for the Company, substantially in the form attached hereto as Exhibit A-3.

(f) The Underwriters shall have received on the Closing Date an opinion of Lando & Anastasi, LLP, special intellectual property counsel for the Company, substantially in the form attached hereto as Exhibit A-4.

(g) The Underwriters shall have received on the Closing Date an opinion of Wilmer Cutler Pickering Hale and Dorr LLP, counsel for the Underwriters, dated the Closing Date, with respect to the issuance and sale of the Shares, the Registration Statement, the Prospectus and any free writing prospectus, the Time of Sale Prospectus (together with any supplement thereto) and other related matters as the Representatives may reasonably require, and the Company shall have furnished to such counsel such documents as they request for the purpose of enabling them to pass upon such matters.

The opinion of Morgan, Lewis & Bockius LLP described in Section 5(c) above shall be rendered to the Underwriters at the request of the Company and shall so state therein.

(h) The Underwriters shall have received, on each of the date hereof and the Closing Date, a letter dated the date hereof or the Closing Date, as the case may be, in form and substance satisfactory to the Underwriters, from Ernst & Young LLP,

independent public accountants, containing statements and information of the type ordinarily included in accountants' "comfort letters" to underwriters with respect to the financial statements and certain financial information contained in the Registration Statement, the Time of Sale Prospectus and the Prospectus; provided that the letter delivered on the Closing Date shall use a "cut-off date" not earlier than the date hereof.

(i) The "lock-up" agreements, each substantially in the form of Exhibit B hereto, between you and all of the shareholders, optionholders, officers and directors of the Company relating to sales and certain other dispositions of shares of Common Stock or certain other securities, delivered to you on or before the date hereof, shall be in full force and effect on the Closing Date.

(j) The underwriters will have received a certificate from the Company's Chief Financial Officer relating to certain financial and statistical data in the form attached here as Exhibit A-5.

(k) The several obligations of the Underwriters to purchase Additional Shares hereunder are subject to the delivery to you on the applicable Option Closing Date of the following:

- (i) a certificate, dated the Option Closing Date and signed by an executive officer of the Company, confirming that the certificate delivered on the Closing Date pursuant to Section 5(b) hereof remains true and correct as of such Option Closing Date;
- (ii) an opinion of Morgan, Lewis & Bockius LLP, outside counsel for the Company, dated the Option Closing Date, relating to the Additional Shares to be purchased on such Option Closing Date and otherwise to the same effect as the opinion required by Section 5(c) hereof;
- (iii) opinions of Hogan Lovells LLP and Hogan Lovells International LLP, special regulatory counsel for the Company, dated the Option Closing Date, relating to the Additional Shares to be purchased on such Option Closing Date and otherwise to the same effect as the opinion required by Section 5(d) hereof;
- (iv) an opinion of Kendall Square IP Strategies, LLC, special intellectual property counsel for the Company, dated the Option Closing Date, relating to the Additional Shares to be purchased on such Option Closing Date and otherwise to the same effect as the opinion required by Section 5(e) hereof;
- (v) an opinion of Lando & Anastasi, LLP, special intellectual property counsel for the Company, dated the Option Closing Date, relating to the Additional Shares to be purchased on such Option Closing Date and otherwise to the same effect as the opinion required by Section 5(f) hereof;

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- (vi) an opinion of Wilmer Cutler Pickering Hale and Dorr LLP, counsel for the Underwriters, dated the Option Closing Date, relating to the Additional Shares to be purchased on such Option Closing Date and otherwise to the same effect as the opinion required by Section 5(g) hereof;
- (vii) a letter dated the Option Closing Date, in form and substance satisfactory to the Underwriters, from Ernst & Young LLP, independent public accountants, substantially in the same form and substance as the letter furnished to the Underwriters pursuant to Section 5(h) hereof; provided that the letter delivered on the Option Closing Date shall use a "cut-off date" not earlier than three business days prior to such Option Closing Date; and
- (viii) such other documents as you may reasonably request with respect to the good standing of the Company, the due authorization and issuance of the Additional Shares to be sold on such Option Closing Date and other matters related to the issuance of such Additional Shares.

6. *Covenants of the Company.* The Company covenants with each Underwriter as follows:

(a) To furnish to you, without charge, three signed copies of the Registration Statement (including exhibits thereto) and for delivery to each other Underwriter a conformed copy of the Registration Statement (without exhibits thereto) and to furnish to you in New York City, without charge, prior to 10:00 a.m. New York City time on the business day next succeeding the date of this Agreement and during the period mentioned in Section 6(e) or 6(f) below, as many copies of the Time of Sale Prospectus, the Prospectus and any supplements and amendments thereto or to the Registration Statement as you may reasonably request.

(b) Before amending or supplementing the Registration Statement, the Time of Sale Prospectus or the Prospectus, to furnish to you a copy of each such proposed amendment or supplement and not to file any such proposed amendment or supplement to which you reasonably object, and to file with the Commission within the applicable period specified in Rule 424(b) under the Securities Act any prospectus required to be filed pursuant to such Rule.

(c) To furnish to you a copy of each proposed free writing prospectus to be prepared by or on behalf of, used by, or referred to by the Company and not to use or refer to any proposed free writing prospectus to which you reasonably object.

(d) Not to take any action that would result in an Underwriter or the Company being required to file with the Commission pursuant to Rule 433(d) under the Securities Act a free writing prospectus prepared by or on behalf of the Underwriter that the Underwriter otherwise would not have been required to file thereunder.

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(e) If the Time of Sale Prospectus is being used to solicit offers to buy the Shares at a time when the Prospectus is not yet available to prospective purchasers and any event shall occur or condition exist as a result of which it is necessary to amend or supplement the Time of Sale Prospectus in order to make the statements therein, in the light of the circumstances, not misleading, or if any event shall occur or condition exist as a result of which the Time of Sale Prospectus conflicts with the information contained in the Registration Statement then on file, or if, in the opinion of counsel for the Underwriters, it is necessary to amend or supplement the Time of Sale Prospectus to comply with applicable law, forthwith to prepare, file with the Commission and furnish, at its own expense, to the Underwriters and to any dealer upon request, either amendments or supplements to the Time of Sale Prospectus so that the statements in the Time of Sale Prospectus as so amended or supplemented will not, in the light of the circumstances when the Time of Sale Prospectus is delivered to a prospective purchaser, be misleading or so that the Time of Sale Prospectus, as amended or supplemented, will no longer conflict with the Registration Statement, or so that the Time of Sale Prospectus, as amended or supplemented, will comply with applicable law.

(f) If, during such period after the first date of the public offering of the Shares as in the opinion of counsel for the Underwriters the Prospectus (or in lieu thereof the notice referred to in Rule 173(a) of the Securities Act) is required by law to be delivered in connection with sales by an Underwriter or dealer, any event shall occur or condition exist as a result of which it is necessary to amend or supplement the Prospectus in order to make the statements therein, in the light of the circumstances when the Prospectus (or in lieu thereof the notice referred to in Rule 173(a) of the Securities Act) is delivered to a purchaser, not misleading, or if, in the opinion of counsel for the Underwriters, it is necessary to amend or supplement the Prospectus to comply with applicable law, forthwith to prepare, file with the Commission and furnish, at its own expense, to the Underwriters and to the dealers (whose names and addresses you will furnish to the Company) to which Shares may have been sold by you on behalf of the Underwriters and to any other dealers upon request, either amendments or supplements to the Prospectus so that the statements in the Prospectus as so amended or supplemented will not, in the light of the circumstances when the Prospectus (or in lieu thereof the notice referred to in Rule 173(a) of the Securities Act) is delivered to a purchaser, be misleading or so that the Prospectus, as amended or supplemented, will comply with applicable law.

(g) To endeavor to qualify the Shares for offer and sale under the securities or Blue Sky laws of such jurisdictions as you shall reasonably request; provided, that in no event shall the Company be obligated to qualify to do business in any jurisdiction where it is not now so qualified or to take any action that would subject it to service of process in suits, other than those arising out of the offering or sale of the Shares, in any jurisdiction where it is now so subject.

(h) To make generally available to the Company's security holders and to you as soon as practicable an earnings statement covering a period of at least twelve months beginning with the first fiscal quarter of the Company occurring after the date of this

Agreement which shall satisfy the provisions of Section 11(a) of the Securities Act and the rules and regulations of the Commission thereunder.

(i) Whether or not the transactions contemplated in this Agreement are consummated or this Agreement is terminated, to pay or cause to be paid all expenses incident to the performance of its obligations under this Agreement, including: (i) the fees, disbursements and expenses of the Company's counsel and the Company's accountants in connection with the registration and delivery of the Shares under the Securities Act and all other fees or expenses in connection with the preparation and filing of the Registration Statement, any preliminary prospectus, the Time of Sale Prospectus, the Prospectus, any free writing prospectus prepared by or on behalf of, used by, or referred to by the Company and amendments and supplements to any of the foregoing, including all printing costs associated therewith, and the mailing and delivering of copies thereof to the Underwriters and dealers, in the quantities hereinabove specified, (ii) all costs and expenses related to the transfer and delivery of the Shares to the Underwriters, including any transfer or other taxes payable thereon, (iii) the cost of printing or producing any Blue Sky or Legal Investment memorandum in connection with the offer and sale of the Shares under state securities laws and all expenses in connection with the qualification of the Shares for offer and sale under state securities laws as provided in Section 6(g) hereof, including filing fees and the reasonable fees and disbursements of counsel for the Underwriters (with such fees and disbursements not to exceed \$5,000) in connection with such qualification and in connection with the Blue Sky or Legal Investment memorandum, (iv) all filing fees and the reasonable fees and disbursements of counsel to the Underwriters (with such fees and disbursements not to exceed \$40,000) incurred in connection with the review and qualification of the offering of the Shares by the Financial Industry Regulatory Authority, (v) all fees and expenses in connection with the preparation and filing of the registration statement on Form 8-A relating to the Common Stock and all costs and expenses incident to listing the Shares on the NASDAQ Global Market, (vi) the cost of printing certificates representing the Shares, (vii) the costs and charges of any transfer agent, registrar or depositary, (viii) the costs and expenses of the Company relating to investor presentations on any "road show" undertaken in connection with the marketing of the offering of the Shares, including, without limitation, expenses associated with the preparation or dissemination of any electronic road show, expenses associated with the production of road show slides and graphics, fees and expenses of any consultants engaged in connection with the road show presentations with the prior approval of the Company, travel and lodging expenses of the representatives and officers of the Company and any such consultants, and 50% of the cost of any aircraft chartered in connection with the road show, provided that no aircraft shall be chartered without the prior consent of the Company, and provided further that, for the avoidance of doubt, the Underwriters shall pay their own travel expenses (including lodging, transportation, meals and entertainment), (ix) the document production charges and expenses associated with printing this Agreement and (x) all other costs and expenses incident to the performance of the obligations of the Company hereunder for which provision is not otherwise made in this Section. It is understood, however, that except as provided in this Section, Section 8 entitled "Indemnity and Contribution" and the last paragraph of Section 10 below, the Underwriters will pay all of their costs and expenses, including fees and disbursements of their counsel, stock transfer taxes payable on resale

of any of the Shares by them and any advertising expenses connected with any offers they may make.

(j) The Company will promptly notify the Representatives if the Company ceases to be an Emerging Growth Company at any time prior to the later of (a) completion of the distribution of the Shares within the meaning of the Securities Act and (b) completion of the Restricted Period (as defined in this Section 6).

(k) If at any time following the distribution of any Written Testing-the-Waters Communication there occurred or occurs an event or development as a result of which such Written Testing-the-Waters Communication included or would include an untrue statement of a material fact or omitted or would omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances existing at that subsequent time, not misleading, the Company will promptly notify the Representatives and will promptly amend or supplement, at its own expense, such Written Testing-the-Waters Communication to eliminate or correct such untrue statement or omission.

The Company also covenants with each Underwriter that, without the prior written consent of the Representatives on behalf of the Underwriters, it will not, during the period ending 180 days after the date of the Prospectus (the “**Restricted Period**”), (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of Common Stock or any securities convertible into or exercisable or exchangeable for Common Stock or (2) enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the Common Stock, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of Common Stock or such other securities, in cash or otherwise or (3) except as otherwise permitted herein, file any registration statement with the Commission relating to the offering of any shares of Common Stock or any securities convertible into or exercisable or exchangeable for Common Stock.

The restrictions contained in the preceding paragraph shall not apply to (1) the Shares to be sold hereunder, (2) the issuance by the Company of shares of Common Stock, or any securities convertible into, or exercisable for, shares of Common Stock, pursuant to any employee stock option plan, incentive plan, employee stock purchase plan or stock ownership plan of the Company in effect on the date hereof and disclosed in the Prospectus, provided that the underlying equity securities shall continue to be subject to the restrictions on transfer set forth in the preceding paragraph during the Restricted Period, (3) the issuance by the Company of shares of Common Stock issuable upon the conversion of securities outstanding on the date hereof, (4) the filing of one or more registration statements on Form S-8, or (5) the offer, issuance and sale of shares of Common Stock or any securities convertible into, or exercisable, or exchangeable for, shares of Common Stock in connection with any acquisition or strategic investment (including any joint venture, strategic alliance or partnership) so long as (x) the aggregate number of shares of Common Stock issued or issuable does not exceed 5% of the number of shares of Common Stock outstanding immediately after the issuance and sale of the

securities, and (y) each recipient of any such shares or other securities agrees to restrictions on the resale of securities that are consistent with the lock-up letters described in Section 5(h) hereof for the remainder of the Restricted Period.

If the Representatives, in their sole discretion, agree to release or waive the restrictions set forth in a lock-up letter described in Section 5(h) hereof for an officer or director of the Company and provide the Company with notice of the impending release or waiver at least three business days before the effective date of the release or waiver, the Company agrees to announce the impending release or waiver by a press release substantially in the form of Exhibit C hereto through a major news service at least two business days before the effective date of the release or waiver.

7. *Covenants of the Underwriters.* Each Underwriter severally covenants with the Company not to take any action that would result in the Company being required to file with the Commission under Rule 433(d) under the Securities Act a free writing prospectus prepared by or on behalf of such Underwriter that otherwise would not be required to be filed by the Company thereunder, but for the action of the Underwriter.

8. *Indemnity and Contribution.* (a) The Company agrees to indemnify and hold harmless each Underwriter, each person, if any, who controls any Underwriter within the meaning of either Section 15 of the Securities Act or Section 20 of the Exchange Act and each affiliate of any Underwriter within the meaning of Rule 405 under the Securities Act from and against any and all losses, claims, damages and liabilities (including, without limitation, any legal or other expenses reasonably incurred in connection with defending or investigating any such action or claim) caused by any untrue statement or alleged untrue statement of a material fact contained in the Registration Statement or any amendment thereof, any preliminary prospectus, the Time of Sale Prospectus or any amendment or supplement thereto, any issuer free writing prospectus as defined in Rule 433(h) under the Securities Act, any Company information that the Company has filed, or is required to file, pursuant to Rule 433(d) under the Securities Act, any road show as defined in Rule 433(h) under the Securities Act (a “road show”), or the Prospectus or any amendment or supplement thereto, or any Written Testing-the-Waters Communication caused by any omission or alleged omission to state therein a material fact required to be stated therein or necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading, except insofar as such losses, claims, damages or liabilities are caused by any such untrue statement or omission or alleged untrue statement or omission based upon information relating to any Underwriter furnished to the Company in writing by such Underwriter through you expressly for use therein. [The Company agrees and confirms that references to “affiliates” of Morgan Stanley that appear in this Agreement shall be understood to include Mitsubishi UFJ Morgan Stanley Securities Co., Ltd.]

(b) Each Underwriter agrees, severally and not jointly, to indemnify and hold harmless the Company, its directors, its officers who sign the Registration Statement and each person, if any, who controls the Company within the meaning of either Section 15 of the Securities Act or Section 20 of the Exchange Act to the same extent as the foregoing indemnity from the Company to such Underwriter, but only with reference to

information relating to such Underwriter furnished to the Company in writing by such Underwriter through you expressly for use in the Registration Statement, any preliminary prospectus, the Time of Sale Prospectus, any issuer free writing prospectus, road show or the Prospectus or any amendment or supplement thereto.

(c) In case any proceeding (including any governmental investigation) shall be instituted involving any person in respect of which indemnity may be sought pursuant to Section 8(a) or 8(b), such person (the “**indemnified party**”) shall promptly notify the person against whom such indemnity may be sought (the “**indemnifying party**”) in writing and the indemnifying party, upon request of the indemnified party, shall retain counsel reasonably satisfactory to the indemnified party to represent the indemnified party and any others the indemnifying party may designate in such proceeding and shall pay the fees and disbursements of such counsel related to such proceeding. In any such proceeding, any indemnified party shall have the right to retain its own counsel, but the fees and expenses of such counsel shall be at the expense of such indemnified party unless (i) the indemnifying party and the indemnified party shall have mutually agreed to the retention of such counsel or (ii) the named parties to any such proceeding (including any impleaded parties) include both the indemnifying party and the indemnified party and representation of both parties by the same counsel would be inappropriate due to actual or potential differing interests between them. It is understood that the indemnifying party shall not, in respect of the legal expenses of any indemnified party in connection with any proceeding or related proceedings in the same jurisdiction, be liable for the fees and expenses of more than one separate firm (in addition to any local counsel) for all such indemnified parties and that all such fees and expenses shall be reimbursed as they are incurred. Such firm shall be designated in writing by the Representatives, in the case of parties indemnified pursuant to Section 8(a), and by the Company, in the case of parties indemnified pursuant to Section 8(b). The indemnifying party shall not be liable for any settlement of any proceeding effected without its written consent, but if settled with such consent or if there be a final judgment for the plaintiff, the indemnifying party agrees to indemnify the indemnified party from and against any loss or liability by reason of such settlement or judgment. Notwithstanding the foregoing sentence, if at any time an indemnified party shall have

requested an indemnifying party to reimburse the indemnified party for fees and expenses of counsel as contemplated by the second and third sentences of this paragraph, the indemnifying party agrees that it shall be liable for any settlement of any proceeding effected without its written consent if (i) such settlement is entered into more than 30 days after receipt by such indemnifying party of the aforesaid request and (ii) such indemnifying party shall not have reimbursed the indemnified party in accordance with such request prior to the date of such settlement. No indemnifying party shall, without the prior written consent of the indemnified party, effect any settlement of any pending or threatened proceeding in respect of which any indemnified party is or could have been a party and indemnity could have been sought hereunder by such indemnified party, unless such settlement includes an unconditional release of such indemnified party from all liability on claims that are the subject matter of such proceeding and does not include a statement as to or an admission of fault, culpability or a failure to act by or on behalf of any indemnified party.

(d) To the extent the indemnification provided for in Section 8(a) or 8(b) is unavailable to an indemnified party or insufficient in respect of any losses, claims, damages or liabilities referred to therein, then each indemnifying party under such paragraph, in lieu of indemnifying such indemnified party thereunder, shall contribute to the amount paid or payable by such indemnified party as a result of such losses, claims, damages or liabilities (i) in such proportion as is appropriate to reflect the relative benefits received by the Company on the one hand and the Underwriters on the other hand from the offering of the Shares or (ii) if the allocation provided by clause 8(d)(i) above is not permitted by applicable law, in such proportion as is appropriate to reflect not only the relative benefits referred to in clause 8(d)(i) above but also the relative fault of the Company on the one hand and of the Underwriters on the other hand in connection with the statements or omissions that resulted in such losses, claims, damages or liabilities, as well as any other relevant equitable considerations. The relative benefits received by the Company on the one hand and the Underwriters on the other hand in connection with the offering of the Shares shall be deemed to be in the same respective proportions as the net proceeds from the offering of the Shares (before deducting expenses) received by the Company and the total underwriting discounts and commissions received by the Underwriters, in each case as set forth in the table on the cover of the Prospectus, bear to the aggregate Public Offering Price of the Shares. The relative fault of the Company on the one hand and the Underwriters on the other hand shall be determined by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or the omission or alleged omission to state a material fact relates to information supplied by the Company or by the Underwriters and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission. The Underwriters' respective obligations to contribute pursuant to this Section 8 are several in proportion to the respective number of Shares they have purchased hereunder, and not joint.

(e) The Company and the Underwriters agree that it would not be just or equitable if contribution pursuant to this Section 8 were determined by *pro rata* allocation (even if the Underwriters were treated as one entity for such purpose) or by any other method of allocation that does not take account of the equitable considerations referred to in Section 8(d). The amount paid or payable by an indemnified party as a result of the losses, claims, damages and liabilities referred to in Section 8(d) shall be deemed to include, subject to the limitations set forth above, any legal or other expenses reasonably incurred by such indemnified party in connection with investigating or defending any such action or claim. Notwithstanding the provisions of this Section 8, no Underwriter shall be required to contribute any amount in excess of the amount by which the total price at which the Shares underwritten by it and distributed to the public were offered to the public exceeds the amount of any damages that such Underwriter has otherwise been required to pay by reason of such untrue or alleged untrue statement or omission or alleged omission. No person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) shall be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation. The remedies provided for in this Section 8 are not exclusive and shall not limit any rights or remedies which may otherwise be available to any indemnified party at law or in equity.

(f) The indemnity and contribution provisions contained in this Section 8 and the representations, warranties and other statements of the Company contained in this Agreement shall remain operative and in full force and effect regardless of (i) any termination of this Agreement, (ii) any investigation made by or on behalf of any Underwriter, any person controlling any Underwriter or any affiliate of any Underwriter or by or on behalf of the Company, its officers or directors or any person controlling the Company and (iii) acceptance of and payment for any of the Shares.

9. *Termination.* The Underwriters may terminate this Agreement by notice given by you to the Company, if after the execution and delivery of this Agreement and prior to the Closing Date (i) trading generally shall have been suspended or materially limited on, or by, as the case may be, any of the New York Stock Exchange, the NYSE MKT, the NASDAQ Global Market, the Chicago Board of Options Exchange, the Chicago Mercantile Exchange or the Chicago Board of Trade, (ii) trading of any securities of the Company shall have been suspended on any exchange or in any over-the-counter market, (iii) a material disruption in securities settlement, payment or clearance services in the United States shall have occurred, (iv) any moratorium on commercial banking activities shall have been declared by Federal or New York State authorities or (v) there shall have occurred any outbreak or escalation of hostilities, or any change in financial markets or any calamity or crisis that, in your judgment, is material and adverse and which, singly or together with any other event specified in this clause (v), makes it, in your judgment, impracticable or inadvisable to proceed with the offer, sale or delivery of the Shares on the terms and in the manner contemplated in the Time of Sale Prospectus or the Prospectus.

10. *Effectiveness; Defaulting Underwriters.* This Agreement shall become effective upon the execution and delivery hereof by the parties hereto.

If, on the Closing Date or an Option Closing Date, as the case may be, any one or more of the Underwriters shall fail or refuse to purchase Shares that it has or they have agreed to purchase hereunder on such date, and the aggregate number of Shares which such defaulting Underwriter or Underwriters agreed but failed or refused to purchase is not more than one-tenth of the aggregate number of the Shares to be purchased on such date, the other Underwriters shall be obligated severally in the proportions that the number of Firm Shares set forth opposite their respective names in Schedule I bears to the aggregate number of Firm Shares set forth opposite the names of all such non-defaulting Underwriters, or in such other proportions as you may specify, to purchase the Shares which such defaulting Underwriter or Underwriters agreed but failed or refused to purchase on such date; *provided* that in no event shall the number of Shares that any Underwriter has agreed to purchase pursuant to this Agreement be increased pursuant to this Section 10 by an amount in excess of one-ninth of such number of Shares without the written consent of such Underwriter. If, on the Closing Date, any Underwriter or Underwriters shall fail or refuse to purchase Firm Shares and the aggregate number of Firm Shares with respect to which such default occurs is more than one-tenth of the aggregate number of Firm Shares to be purchased on such date, and arrangements satisfactory to you and the Company for the purchase of such Firm Shares are not made within 36 hours after such default, this Agreement shall terminate without

liability on the part of any non-defaulting Underwriter or the Company. In any such case either you or the Company shall have the right to postpone the Closing Date, but in no event for longer than seven days, in order that the required changes, if any, in the Registration Statement, in the Time of Sale Prospectus, in the Prospectus or in any other documents or arrangements may be effected. If, on an Option Closing Date, any Underwriter or Underwriters shall fail or refuse to purchase Additional Shares and the aggregate number of Additional Shares with respect to which such default occurs is more than one-tenth of the aggregate number of Additional Shares to be purchased on such Option Closing Date, the non-defaulting Underwriters shall have the option to (i) terminate their obligation hereunder to purchase the Additional Shares to be sold on such Option Closing Date or (ii) purchase not less than the number of Additional Shares that such non-defaulting Underwriters would have been obligated to purchase in the absence of such default. Any action taken under this paragraph shall not relieve any defaulting Underwriter from liability in respect of any default of such Underwriter under this Agreement.

If this Agreement shall be terminated by the Underwriters, or any of them, because of any failure or refusal on the part of the Company to comply with the terms or to fulfill any of the conditions of this Agreement, or if for any reason the Company shall be unable to perform its obligations under this Agreement, the Company will reimburse the Underwriters or such Underwriters as have so terminated this Agreement with respect to themselves, severally, for all out-of-pocket expenses (including the fees and disbursements of their counsel) reasonably incurred by such Underwriters in connection with this Agreement or the offering contemplated hereunder.

11. *Entire Agreement.* (a) This Agreement, together with any contemporaneous written agreements and any prior written agreements (to the extent not superseded by this Agreement) that relate to the offering of the Shares, represents the entire agreement between the Company and the Underwriters with respect to the preparation of any preliminary prospectus, the Time of Sale Prospectus, the Prospectus, the conduct of the offering, and the purchase and sale of the Shares.

(b) The Company acknowledges that in connection with the offering of the Shares: (i) the Underwriters have acted at arm's length, are not agents of, and owe no fiduciary duties to, the Company or any other person, (ii) the Underwriters owe the Company only those duties and obligations set forth in this Agreement and prior written agreements (to the extent not superseded by this Agreement), if any, and (iii) the Underwriters may have interests that differ from those of the Company. The Company waives to the full extent permitted by applicable law any claims it may have against the Underwriters arising from an alleged breach of fiduciary duty in connection with the offering of the Shares.

12. *Counterparts.* This Agreement may be signed in two or more counterparts, each of which shall be an original, with the same effect as if the signatures thereto and hereto were upon the same instrument.

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13. *Applicable Law.* This Agreement shall be governed by and construed in accordance with the internal laws of the State of New York.

14. *Headings.* The headings of the sections of this Agreement have been inserted for convenience of reference only and shall not be deemed a part of this Agreement.

15. *Notices.* All communications hereunder shall be in writing and effective only upon receipt and if to the Underwriters shall be delivered, mailed or sent to you in care of Morgan Stanley & Co. LLC, 1585 Broadway, New York, New York 10036, Attention: Equity Syndicate Desk, with a copy to the Legal Department; and if to the Company shall be delivered, mailed or sent to 500 Boylston Street, 11th Floor, Boston, Massachusetts 02116, attention of the Legal Department.

Very truly yours,

RHYTHM PHARMACEUTICALS, INC.

By:

Name:

Title:

Accepted as of the date hereof

Morgan Stanley & Co. LLC
Merrill Lynch, Pierce, Fenner & Smith
Incorporated
Cowen and Company, LLC

Acting severally on behalf of themselves and
the several Underwriters named in
Schedule I hereto.

By: Morgan Stanley & Co. LLC

By:

Name:

Title:

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By: Merrill Lynch, Pierce, Fenner & Smith
Incorporated

By: _____
Name:
Title:

By: Cowen and Company, LLC

By: _____
Name:
Title:

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SCHEDULE I

<u>Underwriter</u>	<u>Number of Firm Shares To Be Purchased</u>
Morgan Stanley & Co. LLC	
Merrill Lynch, Pierce, Fenner & Smith Incorporated	
Cowen and Company, LLC	
Needham & Company, LLC	
Total:	_____

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SCHEDULE II

Time of Sale Prospectus

1. Preliminary Prospectus issued [date]
 2. [identify all free writing prospectuses filed by the Company under Rule 433(d) of the Securities Act]
 3. [free writing prospectus containing a description of terms that does not reflect final terms, if the Time of Sale Prospectus does not include a final term sheet]
 4. [orally communicated pricing information such as price per share and size of offering if a Rule 134 pricing term sheet is used at the time of sale instead of a pricing term sheet filed by the Company under Rule 433(d) as a free writing prospectus]
-

SCHEDULE III

Schedule of Written Testing-the-Waters Communication

[list all Written Testing-the-Waters Communication]

EXHIBIT A-1

[FORM OF OPINION OF COMPANY COUNSEL]

A-1

EXHIBIT A-2

[FORM OF OPINION OF SPECIAL REGULATORY COUNSEL]

A-2

[FORM OF OPINION OF SPECIAL INTELLECTUAL PROPERTY COUNSEL]

A-3

[FORM OF OPINION OF SPECIAL INTELLECTUAL PROPERTY COUNSEL]

A-4

[FORM OF OFFICER'S CERTIFICATE RE: FINANCIAL AND STATISTICAL DATA]

A-5

[FORM OF LOCK-UP LETTER]

B-1

FORM OF WAIVER OF LOCK-UP

, 20

[Name and Address of
Officer or Director
Requesting Waiver]

Dear Mr./Ms. [Name]:

This letter is being delivered to you in connection with the offering by Rhythm Pharmaceuticals, Inc. (the “**Company**”) of shares of common stock, \$0.001 par value (the “**Common Stock**”), of the Company and the lock-up letter dated [] , 2017 (the “Lock-up Letter”), executed by you in connection with such offering, and your request for a [waiver] [release] dated , 20 , with respect to shares of Common Stock (the “**Shares**”).

Morgan Stanley & Co. LLC, Merrill Lynch, Pierce, Fenner & Smith Incorporated and Cowen and Company, LLC hereby agree to [waive] [release] the transfer restrictions set forth in the Lock-up Letter, but only with respect to the Shares, effective , 20 ; provided, however, that such [waiver] [release] is conditioned on the Company announcing the impending [waiver] [release] by press release through a major news service at least two business days before effectiveness of such [waiver] [release]. This letter will serve as notice to the Company of the impending [waiver] [release].

Except as expressly [waived] [released] hereby, the Lock-up Letter shall remain in full force and effect.

Very truly yours,

Morgan Stanley & Co. LLC
Merrill Lynch, Pierce, Fenner & Smith
Incorporated
Cowen and Company, LLC
Acting severally on behalf of themselves and the several Underwriters named
in Schedule I hereto

By:

Name:

Title:

cc: Company

B-2

FORM OF PRESS RELEASE

Rhythm Pharmaceuticals, Inc.

[Date]

Rhythm Pharmaceuticals, Inc. (the “**Company**”) announced today that Morgan Stanley & Co. LLC, Merrill Lynch, Pierce, Fenner & Smith Incorporated and Cowen and Company, LLC, the lead book-running managers in the Company’s recent public sale of [] shares of common stock are [waiving][releasing] a lock-up restriction with respect to [] shares of the Company’s common stock held by [certain officers or directors] [an officer or director] of the Company. The [waiver][release] will take effect on [], 20 [], and the shares may be sold on or after such date.

This press release is not an offer for sale of the securities in the United States or in any other jurisdiction where such offer is prohibited, and such securities may not be offered or sold in the United States absent registration or an exemption from registration under the United States Securities Act of 1933, as amended.

**BYLAWS
OF
RHYTHM PHARMACEUTICALS, INC.
ARTICLE I
STOCKHOLDERS**

SECTION 1. Place of Meetings. All meetings of stockholders shall be held at the principal office of the corporation or at such other place as may be named in the notice. Notwithstanding the foregoing, the Board of Directors may, in its sole discretion, determine that the meeting shall not be held at any place, but shall be held solely by means of remote communication, subject to such guidelines and procedures as the Board of Directors may adopt, as permitted by applicable law.

SECTION 2. Annual Meeting. The annual meeting of stockholders for the election of directors and the transaction of such other business as may properly come before the meeting shall be held on such date and at such hour and place as the Board of Directors or an officer designated by the Board of Directors may determine. If the annual meeting is not held on the date designated therefor, the Board of Directors shall cause the meeting to be held as soon thereafter as convenient.

SECTION 3. Remote Communication. For the purposes of these bylaws, if authorized by the Board of Directors in its sole discretion, and subject to such guidelines and procedures as the Board of Directors may adopt, stockholders and proxyholders not physically present at a meeting of the stockholders may, by means of remote communication, participate in a meeting of stockholders and be deemed present in person and vote at a meeting of stockholders whether such meeting is to be held at a designated place or solely by means of remote communication, provided that (i) the corporation shall implement reasonable measures to verify that each person deemed present and permitted to vote at the meeting by means of remote communication is a stockholder or proxyholder, (ii) the corporation shall implement reasonable measures to provide such stockholders and proxyholders a reasonable opportunity to participate in the meeting and to vote on matters submitted to the stockholders, including an opportunity to read or hear the proceedings of the meeting substantially concurrently with such proceedings, and (iii) if any stockholder or proxyholder votes or takes other action at the meeting by means of remote communication, a record of such vote or other action shall be maintained by the corporation.

SECTION 4. Special Meetings. Special meetings of the stockholders may be called at any time by the President or a majority of the Board of Directors. A special meeting of stockholders shall be called by the Secretary, upon written request of stockholders who together own of record a majority of the outstanding shares of each class of stock entitled to vote at such meeting.

SECTION 5. Notice of Meetings. Except where some other notice is required by law, notices of meetings of the stockholders shall state the place, if any, date and hour of the meeting, the means of remote communications, if any, by which stockholders and proxyholders may be deemed to be present in person and vote at such meetings and the purposes for which the meeting is called, shall be given by the Secretary under the direction of the Board of Directors or the President, not less than ten nor more than sixty days before the date fixed for such meeting, to each stockholder of record entitled to vote at such meeting. If the Board of Directors has chosen to make a list of stockholders available on an electronic network, the notice shall provide the information required to gain access to such list. Notice to stockholders may be given in writing or by electronic transmission as permitted pursuant to this Section 5. If given in writing, notice shall be given personally to each stockholder or left at such stockholder's residence or usual place of business or mailed postage prepaid and addressed to the stockholder at such stockholder's address as it appears upon the records of the corporation. In case of the death, absence, incapacity or refusal of the Secretary, such notice may be given by a person designated either by the President or the Board of Directors. Only such business shall be conducted at a special meeting of stockholders as shall have been brought before the meeting pursuant to the corporation's notice of meeting. Notice of any meeting of stockholders need not be given to any stockholder who has waived such notice in writing or by electronic transmission, whether before or after the time such meeting is held. Attendance of a person at a meeting of stockholders shall constitute a waiver of notice of such meeting, except when the stockholder attends a meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Neither the business to be transacted at, nor the purpose of, any regular or special meeting of the stockholders need be specified in any written or electronically transmitted waiver of notice. Except as required by statute, notice of any adjourned meeting of the stockholders shall not be required.

Any notice to stockholders given by the corporation shall be effective if given by a form of electronic transmission consented to by the stockholder to whom the notice is given to the extent permitted by applicable law. Any such consent shall be revocable by the stockholder by written notice to the corporation and shall also be deemed revoked if (1) the corporation is unable to deliver by electronic transmission two consecutive notices given by the corporation in accordance with such consent and (2) such inability becomes known to the Secretary or Assistant Secretary of the corporation or to the transfer agent or other person responsible for the giving of notice; provided, however, the inadvertent failure to treat such inability as a revocation shall not invalidate any meeting or other action. Notice given pursuant to this Section shall be deemed given: (1) if by facsimile telecommunication, when directed to a number at which the stockholder has consented to receive notice; (2) if by electronic mail, when directed to an electronic mail address at which the stockholder has consented to receive notice; (3) if by posting on an electronic network together with separate notice to the stockholder of such specific posting, upon the later of (A) such posting and (B) the giving of such separate notice; and (4) if by any other form of electronic transmission consented to by the stockholder, when directed to the stockholder in accordance with such consent. An affidavit of the secretary or an assistant secretary or of the transfer agent or other agent of the corporation that the notice has been given by a form of electronic transmission shall, in the absence of fraud, be prima facie evidence of the facts stated therein.

For purposes of these bylaws, "electronic transmission" means any form of communication, not directly involving the physical transmission of paper, that creates a record that may be retained, retrieved and reviewed by a recipient thereof, and that may be directly reproduced in paper form by such a recipient through an automated process.

SECTION 6. Record Date. The Board of Directors may fix in advance a record date for the determination of the stockholders entitled to notice of or to vote at any meeting of stockholders, or entitled to consent to corporation action in writing without a meeting, or entitled to receive payment of any dividend or other distribution or allotment of any rights, or entitled to exercise any rights in respect of any change, conversion or exchange of stock, or for the purpose of any other lawful action. Such record date shall not be earlier than the date upon which the resolution fixing the record date is adopted by the Board of Directors and shall not be more than 60 nor less than 10 days before the date of such meeting, nor more than 60 days before any other action to which such record date relates. If no record date is fixed, the record date for determining stockholders entitled to notice of or to vote at a meeting of stockholders shall be at the close of business on the day preceding the day on which notice is given, or, if notice is waived, at the close of business on the day preceding the day on which the meeting is held. The record date for determining stockholders for any purpose other than those set forth in this section shall be at the close of business on the day on which the Board of Directors adopts the resolution relating to such purpose. A determination of stockholders of record entitled to notice of or to vote at a meeting of stockholders shall apply to any adjournment of the meeting; provided, however, that the Board of Directors may fix a new record date for the adjourned meeting.

SECTION 7. Voting List. The officer who has charge of the stock ledger of the corporation shall make or have made, at least 10 days before every meeting of stockholders, a complete list of the stockholders entitled to vote at the meeting, arranged in alphabetical order and showing the address of each stockholder and the number of shares registered in the name of each stockholder. Such list shall be open to the examination of any stockholder for any purpose germane to the meeting, during ordinary business hours, for a period of at least 10 days before the meeting either on a reasonably accessible electronic network or during ordinary business hours at the principal place of business of the corporation. The list shall also be produced and kept at the time and place of the meeting during the whole time thereof, and may be inspected by any stockholder who is present. The stock ledger shall be the only evidence as to who are the stockholders entitled to examine the stock ledger, the list required by this section or the books of the corporation, or to vote at any meeting of stockholders.

SECTION 8. Quorum of Stockholders. Unless otherwise provided in the Certificate of Incorporation, at any meeting of the stockholders, the holders of a majority of the voting power of the outstanding shares of capital stock of the corporation entitled to vote generally in the election of directors present in person or represented by proxy, shall constitute a quorum for the consideration of any question, but in the absence of a quorum a smaller group may adjourn any meeting from time to time. When a quorum is present at any meeting, a majority of the votes properly cast shall, except where a different vote is required by law, by the Certificate of Incorporation or by these bylaws, decide any question brought before such meeting. Any election by stockholders shall be determined by a plurality of the vote cast by the stockholders entitled to vote at the election. The stockholders present at a duly organized meeting may

continue to transact business until adjournment, notwithstanding the withdrawal of enough stockholders to leave less than a quorum.

SECTION 9. Proxies and Voting. Unless otherwise provided in the Certificate of Incorporation, each stockholder entitled to vote at a meeting of stockholders may authorize another person or persons to act for such stockholder by proxy, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period. Shares of the capital stock of the corporation belonging to the corporation or to another corporation, a majority of whose shares entitled to vote in the election of directors is owned by the corporation, shall neither be entitled to vote nor be counted for quorum purposes.

SECTION 10. Conduct of Meeting. Meetings of the stockholders shall be presided over by the Chairman of the Board, if any, or in the absence of the Chairman of the Board by the Vice Chairman of the Board, if any, or in the absence of the Vice Chairman of the Board by the President, or in the absence of the President by a Vice-President, or in the absence of the foregoing persons by a chairman designated by the Board of Directors, or in the absence of such designation by a chairman chosen at the meeting. The Secretary, or in the absence of the Secretary an Assistant Secretary, shall act as secretary of the meeting, but in the absence of the Secretary and any Assistant Secretary the chairman of the meeting may appoint any person to act as secretary of the meeting.

The Board of Directors may adopt such rules, regulations and procedures for the conduct of the meeting of stockholders as it shall deem appropriate. Except to the extent inconsistent with such rules and regulations as adopted by the Board of Directors, the chairman of the meeting shall have the right and authority to prescribe such rules, regulations and procedures and to do all such acts as, in the judgment of such chairman, are appropriate for the proper conduct of the meeting. Such rules, regulations or procedures, whether adopted by the Board of Directors or prescribed by the chairman of the meeting, may include, without limitation, (i) the establishment of an agenda or order of business for the meeting, (ii) rules and procedures for maintaining order at the meeting and the safety of those present, (iii) limitations on attendance at or participation in the meeting to stockholders of record of the corporation, their duly authorized and constituted proxies or such other persons as the chairman of the meeting shall determine, (iv) restrictions on entry to the meeting after the time fixed for the commencement thereof, and (v) limitations on the time allotted to questions or comments by participants. Unless and to the extent determined by the Board of Directors or the chairman of the meeting, meetings of stockholders shall not be required to be held in accordance with the rules of parliamentary procedure.

SECTION 11. Action Without Meeting. Any action required or permitted to be taken at any annual or special meeting of stockholders of the corporation may be taken without a meeting, without prior notice and without a vote, if a consent in writing, setting forth the action so taken, is signed by the holders or by proxy for the holders of outstanding stock having not less than the minimum number of votes that would be necessary to authorize or take such action at a meeting at which all shares entitled to vote on such action were present and voted. Prompt notice of the taking of corporate action without a meeting by less than unanimous written consent shall be given to those stockholders who have not consented in writing.

SECTION 1. **General Powers.** The business and affairs of the corporation shall be managed by or under the direction of a Board of Directors, who may exercise all of the powers of the corporation that are not by law required to be exercised by the stockholders. In the event of a vacancy on the Board of Directors, the remaining directors, except as otherwise provided by law or the Certificate of Incorporation, may exercise the powers of the full Board until the vacancy is filled.

SECTION 2. **Election.** Subject to the provisions of the Certificate of Incorporation, the holders of record of the capital stock of the corporation, voting as a single class, shall be entitled to elect the directors of the Corporation.

SECTION 3. **Vacancies.** Any vacancy in the Board of Directors, however occurring, including a vacancy resulting from an enlargement of the Board or from the removal of any director, may be filled by vote of a majority of the directors then in office although less than a quorum, or by the sole remaining director. Each director so chosen to fill a vacancy shall serve for a term determined in the manner provided in the Certificate of Incorporation and the General Corporation Law of the State of Delaware. When one or more directors shall resign from the Board, effective at a future date, a majority of the directors then in office, including those who have so resigned, shall have the power to fill such vacancy or vacancies, the vote thereon to take effect when such resignation or resignations shall become effective. If at any time there are no directors in office, then an election of directors may be held in accordance with the General Corporation Law of the State of Delaware.

SECTION 4. **Resignation.** Any director may resign at any time by giving notice to the corporation in writing or by electronic transmission. Such resignation shall take effect at the time specified therein, or if no time is specified, at the time of its receipt by the Chairman of the Board, if any, the President or the Secretary.

SECTION 5. **Removal.** Subject to the provisions of the Certificate of Incorporation, directors may be removed from office only by the holders of record of the capital stock of the corporation, voting as a single class.

SECTION 6. **Committees.** The Board of Directors may, by resolution or resolutions passed by a majority of the whole Board of Directors, designate one or more committees, each committee to consist of one or more directors of the corporation. The Board of Directors may designate one or more directors as alternate members of any committee to replace any absent or disqualified member at any meeting of the committee. In the absence or disqualification of any member of any such committee, the member or members thereof present at any meeting and not disqualified from voting, whether or not such member or members constitute a quorum, may unanimously appoint another member of the Board of Directors to act at the meeting in the place of such absent or disqualified member. The Board of Directors shall have the power to change the members of any such committee at any time, to fill vacancies therein and to discharge any such committee, either with or without cause, at any time.

Any such committee, to the extent permitted by law and to the extent provided in a resolution of the Board of Directors or in these bylaws, shall have and may exercise all the powers and authority of the Board of Directors in the management of the business and affairs of the corporation, and may authorize the seal of the corporation to be affixed to all papers that may require it.

A majority of all the members of any such committee may fix its rules of procedure, determine its actions and fix the time and place, whether within or without the State of Delaware, of its meetings and specify what notice thereof, if any, shall be given, unless the Board of Directors shall otherwise by resolution provide. Each committee shall keep regular minutes of its meetings and make such reports as the Board of Directors may from time to time request.

SECTION 7. **Meetings of the Board of Directors.** Regular meetings of the Board of Directors may be held without call or formal notice at such places either within or without the State of Delaware and at such times as the Board may by vote from time to time determine. A regular meeting of the Board of Directors may be held without call or formal notice immediately after and at the same place as the annual meeting of the stockholders, or any special meeting of the stockholders at which a Board of Directors is elected.

Special meetings of the Board of Directors may be held at any place either within or without the State of Delaware at any time when called by the Chairman of the Board, if any, the President, the Secretary or two or more directors. Reasonable notice of the time and place of a special meeting shall be given to each director unless such notice is waived by attendance or by waiver in the manner provided in these bylaws for waiver of notice by stockholders. Notice may be given by, or by a person designated by, the Secretary, the person or persons calling the meeting, or the Board of Directors. No notice of any adjourned meeting of the Board of Directors shall be required. In any case it shall be deemed sufficient notice to a director to send notice by mail at least seventy-two hours, by telegram or fax at least forty-eight hours before the meeting, addressed to such director at his or her usual or last known business or home address, by electronic mail at least twenty-four hours before the meeting, when directed to his or her usual or last known electronic mail address, or by any other form of electronic transmission to which such director has consented, when directed to the director consistent therewith.

Directors or members of any committee may participate in a meeting of the Board of Directors or of such committee by means of conference telephone or similar communications equipment by means of which all persons participating in the meeting can hear each other, and participation by such means shall constitute presence in person at such meeting.

SECTION 8. **Quorum and Voting.** A majority of the total number of directors shall constitute a quorum, except that when a vacancy or vacancies exist in the Board, a majority of the directors then in office (but not less than one-third of the total number of the directors) shall constitute a quorum. A majority of the directors present, whether or not a quorum is present, may adjourn any meeting from time to time. If, at any meeting, a quorum is not present for any reason, then another Board meeting may be convened within not less than two (2) and not more than ten (10) business days after such meeting and, at such other meeting, a majority of all directors shall constitute a quorum for all purposes. The vote of a majority of the directors present at any meeting at which a quorum is present shall be the act of the Board of Directors,

except where a different vote is required by law, by the Certificate of Incorporation or by these bylaws.

SECTION 9. **Compensation.** The Board of Directors may fix fees for their services and for their membership on committees, and expenses of attendance may be allowed for attendance at each meeting. Nothing herein contained shall be construed to preclude any director from serving the corporation

in any other capacity, as an officer, agent or otherwise, and receiving compensation therefor.

SECTION 10. Action Without Meeting. Any action required or permitted to be taken at any meeting of the Board of Directors or of any committee thereof may be taken without a meeting and without notice if all members of the Board of Directors or of such committee, as the case may be, consent thereto in writing (which may be in counterparts) or by electronic transmission, and the writing or writings or electronic transmission or electronic transmissions are filed with the minutes of proceedings of the Board of Directors or of such committee. Such filings shall be in paper form if the minutes are maintained in paper form and shall be in electronic form if the minutes are maintained in electronic form.

ARTICLE III

OFFICERS

SECTION 1. Titles. The officers of the corporation shall consist of a President, a Secretary, a Treasurer and such other officers with such other titles as the Board of Directors shall determine, who may include without limitation a Chairman of the Board, a Vice-Chairman of the Board and one or more Vice-Presidents, Assistant Treasurers or Assistant Secretaries.

SECTION 2. Election and Term of Office. The officers of the corporation shall be elected from time to time by the Board of Directors to hold office until his or her successor is elected and qualified, unless a different term is specified in the vote electing such officer, or until his or her earlier death, resignation or removal.

SECTION 3. Qualification. Unless otherwise provided by resolution of the Board of Directors, no officer, other than the Chairman or Vice-Chairman of the Board, need be a director. No officer need be a stockholder. Any number of offices may be held by the same person, as the Board of Directors shall determine.

SECTION 4. Removal. Any officer may be removed, with or without cause, at any time, by resolution adopted by the Board of Directors.

SECTION 5. Resignation. Any officer may resign by delivering a written notice to the corporation at its principal office or to the Chairman of the Board, if any, the President or the Secretary. Such resignation shall take effect at the time specified therein, or if no time is specified, at the time of its receipt by the Chairman of the Board, if any, the President or the Secretary.

SECTION 6. Vacancies. The Board of Directors, the Chairman of the Board, if any, or the President may at any time fill any vacancy occurring in any office for the unexpired portion

of the term or may leave unfilled any office other than those of President, Treasurer and Secretary.

SECTION 7. Powers and Duties. The officers of the corporation shall have such powers and perform such duties as are specified herein and as may be conferred upon or assigned to them by the Board of Directors, or, in the case of any officer other than the President, the President, and shall have such additional powers and duties as are incident to their office except to the extent that resolutions of the Board of Directors are inconsistent therewith.

SECTION 8. President and Vice-Presidents. Except to the extent that such duties are assigned by the Board of Directors to the Chairman of the Board, or in the absence of the Chairman or in the event of his or her inability or refusal to act, the President shall be the chief executive officer of the corporation and shall have general and active management of the business of the corporation and general supervision of its officers, agents and employees, and shall see that all orders and resolutions of the Board of Directors are carried into effect. The President shall preside at each meeting of the stockholders and the Board of Directors unless a Chairman or Vice-Chairman of the Board is elected by the Board and is assigned the duty of presiding at such meetings.

The Board of Directors may assign to any Vice-President the title of Executive Vice-President, Senior Vice-President or any other title selected by the Board of Directors. In the absence of the President or in the event of his or her inability or refusal to act, the duties of the President shall be performed by the Executive Vice President, if any, Senior Vice President, if any, or Vice President, if any, in that order (and, in the event there be more than one person in any such office, in the order of their length of time spent in such office), and when so acting, such officer shall have all the powers of and be subject to all the restrictions upon the President.

SECTION 9. Secretary and Assistant Secretaries. The Secretary shall attend all meetings of the Board of Directors and of the stockholders and record all the proceedings of such meetings in a book to be kept for that purpose, shall give, or cause to be given, notice of all meetings of the stockholders and special meetings of the Board of Directors, shall maintain a stock ledger and prepare lists of stockholders and their addresses as required and shall have custody of the corporate seal, which the Secretary or any Assistant Secretary shall have authority to affix to any instrument requiring it and attest by any of their signatures. The Board of Directors may give general authority to any other officer to affix and attest the seal of the corporation.

Any Assistant Secretary, or any other officer, employee or agent designated by the Board of Directors, the Chairman of the Board or the President, may, in the absence of the Secretary or in the event of the Secretary's inability or refusal to act, perform the duties and exercise the powers of the Secretary.

SECTION 10. Treasurer and Assistant Treasurers. The Treasurer shall have the custody of the corporate funds and securities, shall keep full and accurate accounts of receipts and disbursements in books belonging to the corporation and shall deposit all moneys and other valuable effects in the name and to the credit of the corporation in such depositories as may be designated by or pursuant to resolution of the Board of Directors. The Treasurer shall disburse

the funds of the corporation as may be ordered by the Board of Directors, the Chairman of the Board, if any, or the President, taking proper vouchers for such disbursements, and shall render to the Chairman of the Board, if any, the President and the Board of Directors, at its regular meetings or whenever they may require it, an account of all transactions and of the financial condition of the corporation.

Any Assistant Treasurer, or any other officer, employee or agent designated by the Board of Directors, the Chairman of the Board or the President, may, in the absence of the Treasurer or in the event of his or her inability or refusal to act, perform the duties and exercise the powers of the Treasurer.

SECTION 11. Bonded Officers. The Board of Directors may require any officer to give the corporation a bond in such sum and with such surety or sureties as shall be satisfactory to the Board of Directors upon such terms and conditions as the Board of Directors may specify, including without limitation a bond for the faithful performance of the duties of such officer and for the restoration to the corporation of all property in his or her possession or control belonging to the corporation.

ARTICLE IV

STOCK

SECTION 1. Certificates of Stock. Unless otherwise provided by the Board of Directors, the shares of the corporation shall be represented by certificates. One or more stock certificates, signed by (i) the Chairman or Vice-Chairman of the Board of Directors or the President or a Vice-President and (ii) the Treasurer or an Assistant Treasurer or the Secretary or an Assistant Secretary, shall be issued to each stockholder certifying the number of shares owned by the stockholder in the corporation. Any or all signatures on any such certificate may be facsimiles. In case any officer, transfer agent or registrar who shall have signed or whose facsimile signature shall have been placed upon a certificate shall have ceased to be such officer, transfer agent or registrar before such certificate is issued, it may be issued by the corporation with the same effect as if such person or entity were such officer, transfer agent or registrar at the date of issue.

Each certificate for shares of stock that are subject to any restriction on transfer pursuant to the Certificate of Incorporation, these bylaws, applicable securities laws, or any agreement among any number of stockholders or among such holders and the corporation shall have conspicuously noted on the face or back of the certificate either the full text of the restriction or a statement of the existence of such restriction. If the corporation is authorized to issue more than one class or series of stock, each certificate for shares of stock shall have conspicuously noted on the face or back of the certificate a statement that the corporation will furnish without additional charge to each stockholder who so requests the powers, designations, preferences and relative, participating, optional, or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights.

SECTION 2. Transfers of Shares of Stock. Subject to the restrictions, if any, stated or noted on a stock certificate, shares of stock represented by a certificate may be transferred on the

books of the corporation by the surrender to the corporation or its transfer agent of the certificate representing such shares properly endorsed or accompanied by a written assignment or power of attorney properly executed, and with such proof of authority or the authenticity of signature as the corporation or its transfer agent may reasonably require. The corporation shall be entitled to treat the record holder of stock as shown on its books as the owner of such stock for all purposes, including the payment of dividends and the right to vote with respect to that stock, regardless of any transfer, pledge or other disposition of that stock, until the shares have been transferred on the books of the corporation in accordance with the requirements of these bylaws.

SECTION 3. Lost Certificates. A new stock certificate may be issued in the place of any certificate theretofore issued by the corporation and alleged to have been lost, stolen or destroyed, upon such terms in conformity with law as the Board of Directors shall prescribe. The Board of Directors may, in their discretion, require the owner of the lost, stolen or destroyed certificate, or the owner's legal representatives, to give the corporation a bond, in such sum as they may direct, to indemnify the corporation against any claim that may be made against it on account of the alleged loss, theft or destruction of any such certificate, or the issuance of any such new certificate.

SECTION 4. Fractional Share Interests. The corporation may, but shall not be required to, issue fractions of a share. If the corporation does not issue fractions of a share, it shall (i) arrange for the disposition of fractional interests by those entitled thereto, (ii) pay in cash the fair value of fractions of a share as of the time when those entitled to receive such fractions are determined, or (iii) issue scrip or warrants in registered or bearer form, which shall entitle the holder to receive a certificate for a full share upon the surrender of such scrip or warrants aggregating a full share. A certificate for a fractional share shall, but scrip or warrants shall not unless otherwise provided therein, entitle the holder to exercise voting rights, to receive dividends thereon, and to participate in any of the assets of the corporation in the event of liquidation. The Board of Directors may cause scrip or warrants to be issued subject to the conditions that they shall become void if not exchanged for certificates representing full shares before a specified date, or subject to the conditions that the shares for which scrip or warrants are exchangeable may be sold by the corporation and the proceeds thereof distributed to the holders of scrip or warrants, or subject to any other conditions that the Board of Directors may impose.

SECTION 5. Dividends. Subject to the provisions of the Certificate of Incorporation, the Board of Directors may, out of funds legally available therefor declare and pay dividends upon the capital stock of the corporation as and when they deem expedient.

ARTICLE V

INDEMNIFICATION OF DIRECTORS AND OFFICERS

The corporation shall indemnify, to the extent permitted by applicable law, any person made, or threatened to be made, a party to any action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that such person is or was a director or officer of the corporation or serves or served at the request of the corporation as a director or officer of any other enterprise or in a comparable role at such enterprise. Expenses (including attorneys' fees), judgments, fines and amounts paid in settlement, actually and reasonably

incurred by any such person in connection with any such action, suit or proceeding shall be paid or reimbursed by the corporation promptly upon receipt by it of an undertaking of such person to repay such amounts if it shall ultimately be determined that such person is not entitled to be indemnified by the corporation. The rights provided to any person by this bylaw shall be enforceable against the corporation by such person, who shall be presumed to have relied upon it in serving or continuing to serve as a director or officer, and by such person's heirs and legal representations. No amendment, termination or

repeal of this bylaw shall impair the rights of any person arising at any time with respect to actions, transactions or events occurring, or circumstances existing, before such amendment, termination or repeal. For purposes of this bylaw, the term "corporation" shall include any predecessor of the corporation and any constituent corporation (including any constituent of a constituent) absorbed by the corporation in a consolidation or merger; the term "other enterprise" shall include employee benefit plans; the term "fines" shall include any excise taxes assessed on a person with respect to any employee benefit plan; service "at the request of the corporation" shall include service as a director or officer of the corporation which imposes duties on, or involves services by, such director or officer with respect to an employee benefit plan, its participants or beneficiaries; and action by a person with respect to an employee benefit plan which such person reasonably believes to be in the interest of the participants and beneficiaries of such plan shall be deemed to be action not opposed to the best interests of the corporation.

ARTICLE VI

GENERAL PROVISIONS

SECTION 1. Fiscal Year. Except as otherwise designated from time to time by the Board of Directors, the fiscal year of the corporation shall begin on the first day of January and end on the last day of December.

SECTION 2. Corporate Seal. The corporate seal shall be in such form as shall be approved by the Board of Directors. The Secretary shall be the custodian of the seal, and a duplicate seal may be kept and used by each Assistant Secretary and by any other officer the Board of Directors may authorize.

SECTION 3. Certificate of Incorporation. All references in these bylaws to the Certificate of Incorporation shall be deemed to refer to the Certificate of Incorporation of the corporation, as in effect from time to time.

SECTION 4. Execution of Instruments. The President, the Treasurer and the Secretary shall have power to execute and deliver on behalf and in the name of the corporation any instrument requiring the signature of an officer of the corporation, including deeds, contracts, mortgages, bonds, notes, debentures, checks, drafts and other orders for the payment of money. In addition, the Board of Directors, the President, the Treasurer and the Secretary may expressly delegate such powers to any other officer or agent of the corporation.

SECTION 5. Voting of Securities. The President, the Treasurer and the Secretary, and each other person authorized by the Board of Directors, each acting singly, may waive notice of, and act as, or appoint any person or persons to act as, proxy or attorney-in-fact for this

corporation (with or without power of substitution) at any meeting of stockholders or owners of other interests of any other corporation or organization the securities of which may be held by this corporation. In addition, the Board of Directors, the President and the Treasurer may expressly delegate such powers to any other officer or agent of the corporation.

SECTION 6. Evidence of Authority. A certificate by the Secretary, an Assistant Secretary or a temporary secretary as to any action taken by the stockholders, directors, a committee or any officer or representative of the corporation shall, as to all persons who rely on the certificate in good faith, be conclusive evidence of that action.

SECTION 7. Books and Records. The books and records of the corporation shall be kept at such places within or without the State of Delaware as the Board of Directors may from time to time determine.

SECTION 8. Amendments. Subject to any vote of the holders of any class or series of capital stock of the corporation required by the Delaware General Corporation Law or by the Certificate of Incorporation, the Board of Directors is expressly empowered to adopt, amend or repeal the bylaws of the corporation.

Adopted by the Incorporator of the Corporation on February 26, 2013.

**AMENDED AND RESTATED
CERTIFICATE OF INCORPORATION OF
RHYTHM PHARMACEUTICALS, INC.**

Rhythm Pharmaceuticals, Inc., a corporation organized and existing under the laws of the State of Delaware (the “Corporation”), **DOES HEREBY CERTIFY:**

FIRST: The name of the Corporation is “Rhythm Pharmaceuticals, Inc.” The date of filing the original Certificate of Incorporation of the Corporation with the Secretary of State of the State of Delaware was February 26, 2013 under the name “Rhythm Metabolic, Inc.”.

SECOND: This Amended and Restated Certificate of Incorporation (this “Restated Certificate”) has been duly approved by the Board of Directors of the Corporation.

THIRD: This Restated Certificate has been duly adopted by the stockholders of the Corporation in accordance with the provisions of Sections 228, 242 and 245 of the General Corporation Law of the State of Delaware (the “DGCL”), and notice thereof has been given in accordance with the provisions of Section 228 of the DGCL.

FOURTH: The Certificate of Incorporation of this Corporation is hereby amended, integrated and restated to read as follows:

ARTICLE ONE

The name of the Corporation is Rhythm Pharmaceuticals, Inc.

ARTICLE TWO

The address of the Corporation’s registered office is 251 Little Falls Drive, in the City of Wilmington, New Castle County, Delaware 19808. The name of the registered agent at such address is Corporation Service Company.

ARTICLE THREE

The nature of the business or purpose of the Corporation is to engage in any lawful act or activity for which corporations may be organized under the DGCL.

ARTICLE FOUR

Section 1. Authorized Shares. The total number of shares of all classes of capital stock which the Corporation shall have authority to issue is One Hundred Thirty Million (130,000,000) shares, consisting of:

- (a) One Hundred Twenty Million (120,000,000) shares of common stock, par value \$0.001 per share (“Common Stock”); and
- (b) Ten Million (10,000,000) shares of undesignated preferred stock, par value \$0.001 per share (the “Preferred Stock”).

Such stock may be issued from time to time by the Corporation for such consideration as may be fixed by the board of directors of the Corporation (the “Board of Directors”). The following is a statement

of the powers, designations, preferences, privileges, and relative rights in respect of each class of capital stock of the Corporation.

Section 2. Common Stock.

(a) General. The voting, dividend and liquidation rights of the holders of Common Stock are subject to and qualified by the rights of the holders of Preferred Stock.

(b) Voting. Except as otherwise provided by the DGCL or this Restated Certificate and subject to the rights of holders of any series of Preferred Stock, all of the voting power of the stockholders of the Corporation shall be vested in the holders of the Common Stock, and each holder of Common Stock shall have one vote for each share held by such holder on all matters voted upon by the stockholders of the Corporation; provided, however, that, except as otherwise required by law, holders of Common Stock, as such, shall not be entitled to vote on any amendment to this Restated Certificate (or on any amendment to a certificate of designations of any series of Preferred Stock) that alters or changes the powers, preferences, rights or other terms of one or more outstanding series of Preferred Stock if the holders of such affected series of Preferred Stock are entitled to vote, either separately or together with the holders of one or more other such series, on such amendment pursuant to this Restated Certificate (or pursuant to a certificate of designations of any series of Preferred Stock) or pursuant to the DGCL. There shall be no cumulative voting.

(c) Dividends. Except as otherwise provided by the DGCL or this Restated Certificate, dividends may be declared and paid on the Common Stock from funds lawfully available therefor if, as and when determined by the Board of Directors and subject to any preferential dividend rights of any then outstanding shares of Preferred Stock.

(d) No Preemptive Rights. The holders of the Common Stock shall have no preemptive rights to subscribe for any shares of any class of stock of the Corporation whether now or hereafter authorized.

(e) No Conversion Rights. The Common Stock shall not be convertible into, or exchangeable for, shares of any other class or classes or of any other series of the same class of the Corporation’s capital stock.

(f) **Liquidation.** Upon the dissolution or liquidation or winding up of the affairs of the Corporation, whether voluntary or involuntary, holders of Common Stock will be entitled to receive all assets of the Corporation available for distribution to its stockholders equally on a per share basis, subject to any preferential rights of any then outstanding shares of Preferred Stock and after payment or provision for payment of the Corporation's debts.

Section 3. **Preferred Stock.** To the fullest extent authorized by the DGCL, shares of Preferred Stock may be issued from time to time in one or more series, each of such series to have such powers, designations, preferences, and relative, participating, optional, or other special rights, if any, and such qualifications and restrictions, if any, as are stated or expressed in the resolution or resolutions of the Board of Directors providing for such series of Preferred Stock. Different series of Preferred Stock shall not be construed to constitute different classes of shares for the purposes of voting by classes unless expressly so provided in such resolution or resolutions.

Authority is hereby granted to the Board of Directors, acting by resolution or resolutions adopted at any time and from time to time, to create, provide for, designate and issue, out of the authorized but unissued shares of Preferred Stock, one or more series of Preferred Stock, and, in connection with the

creation of any such series of Preferred Stock, to determine and fix the powers, designations, preferences, and relative, participating, optional, or other special rights, if any, and the qualifications and restrictions, if any, including without limitation dividend rights, conversion rights, voting rights (if any), redemption privileges, and liquidation preferences, of such series of Preferred Stock (which need not be uniform among series), all to the fullest extent now or hereafter permitted by the DGCL. Without limiting the generality of the foregoing, the resolution or resolutions providing for the creation or issuance of any series of Preferred Stock may provide that such series shall be superior to, rank equally with, or be junior to any other series of Preferred Stock, all to the fullest extent permitted by law. No resolution, vote, or consent of the holders of the capital stock of the Corporation shall be required in connection with the creation or issuance of any shares of any series of Preferred Stock authorized by and complying with the conditions of this Restated Certificate, the right to any such resolution, vote, or consent being expressly waived by all present and future holders of the capital stock of the Corporation.

Any resolution or resolutions adopted by the Board of Directors pursuant to the authority vested in them by this Section 3 of Article Four shall be set forth in a certificate of designation along with the number of shares of such series of Preferred Stock as to which the resolution or resolutions shall apply and such certificate shall be executed, acknowledged, filed, recorded, and shall become effective, in accordance with Section 103 of the DGCL. Unless otherwise provided in any such resolution or resolutions, the number of shares of any such series of Preferred Stock to which such resolution or resolutions apply may be increased (but not above the total number of authorized shares of Preferred Stock) or decreased (but not below the number of shares of such series of Preferred Stock then outstanding) by a certificate likewise executed, acknowledged, filed and recorded, setting forth a statement that a specified increase or decrease therein has been authorized and directed by a resolution or resolutions likewise adopted by the Board of Directors. In case the number of such shares shall be decreased, the number of shares so specified in the certificate shall resume the status which they had prior to the adoption of the first resolution or resolutions. When no shares of any such series of Preferred Stock are outstanding, either because none were issued or because none remain outstanding, a certificate setting forth a resolution or resolutions adopted by the Board of Directors that none of the authorized shares of such series of Preferred Stock are outstanding, and that none will be issued subject to the certificate of designations previously filed with respect to such series of Preferred Stock, may be executed, acknowledged, filed and recorded in the same manner as previously described and it shall have the effect of eliminating from this Restated Certificate all matters set forth in the certificate of designations with respect to such series of Preferred Stock. If no shares of any such series of Preferred Stock established by a resolution or resolutions adopted by the Board of Directors have been issued, the voting powers, designations, preferences and relative, participating, optional or other rights, if any, with the qualifications, limitations or restrictions thereof, may be amended by a resolution or resolutions adopted by the Board of Directors. In the event of any such amendment, a certificate which (i) states that no shares of such series of Preferred Stock have been issued, (ii) sets forth the copy of the amending resolution or resolutions and (iii) if the designation of such series of Preferred Stock is being changed, indicates the original designation and the new designation, shall be executed, acknowledged, filed, recorded, and shall become effective, in accordance with Section 103 of the DGCL.

ARTICLE FIVE

The Corporation is to have perpetual existence.

ARTICLE SIX

Section 1. **Classification of Directors.** Effective as of the closing (the "IPO Closing") of the Corporation's first public offering of shares of Common Stock registered pursuant to the Securities Act of 1933, as amended, the Board of Directors shall be divided into three classes of directors, Class I, Class II,

and Class III, such classes to be as nearly equal in number of directors as possible, having staggered three-year terms of office (except to the extent otherwise provided in the next sentence with respect to the initial terms of such classes of directors). The initial term of office of the directors of Class I shall expire as of the first annual meeting of the Corporation's stockholders following the IPO Closing; the initial term of office of the directors of Class II shall expire as of the second annual meeting of the Corporation's stockholders following the IPO Closing; and the initial term of office of the directors of Class III shall expire as of the third annual meeting of the Corporation's stockholders following the IPO Closing. At each annual meeting of stockholders of the Corporation after the IPO Closing, nominees will stand for election to succeed those directors whose terms are to expire as of such annual meeting of stockholders, and such nominees elected at such annual meeting of stockholders shall be elected for a term expiring at the third annual meeting of stockholders following their election. Directors shall hold office until the annual meeting of stockholders in which their term is scheduled to expire as set forth above in this Section 1 of Article Six and until their respective successors are duly elected or qualified or until their earlier death, incapacity, resignation or removal. Those directors already in office immediately prior to the IPO Closing shall be allocated among the three classes of directors contemplated under this Section 1 of Article Six pursuant to a resolution or resolutions adopted by the Board of Directors prior to the IPO Closing.

Section 2. **Removal.** Subject to the special rights of the holders of any series of Preferred Stock to elect directors, the directors of the Corporation may be removed only for cause by the affirmative vote of the holders of at least seventy-five percent (75%) of the outstanding shares of capital stock of the

Corporation entitled to vote in the election of directors or class of directors, voting together as a single class, at a meeting of the stockholders called for that purpose.

Section 3. Vacancies. Except as the DGCL may otherwise require, any new directorships or vacancies in the Board of Directors, including new directorships resulting from any increase in the number of directors to serve in the Board of Directors and/or any unfilled vacancies by reason of death, resignation, disqualification, removal for cause, failure to elect or otherwise with respect to any director, may be filled only by the vote of a majority of the remaining directors then in office, although less than a quorum, or by the sole remaining director.

Section 4. Number of Directors. Subject to the special rights of the holders of any series of Preferred Stock to elect directors, the number of directors which shall constitute the Board of Directors shall be fixed exclusively by the Board of Directors from time to time in accordance with the by-laws of the Corporation. No decrease in the number of directors constituting the whole board shall shorten the term of any incumbent director.

ARTICLE SEVEN

The Board of Directors shall have the power and authority: (i) to adopt, amend or repeal the Corporation's by-laws, subject to the power of the stockholders of the Corporation entitled to vote with respect thereto to make, alter, amend or repeal the by-laws; provided, that with respect to the powers of stockholders entitled to vote with respect thereto to make, alter, amend or repeal the by-laws, in addition to any other vote otherwise required by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the outstanding shares of capital stock of the Corporation entitled to vote in the election of directors or class of directors, voting together as a single class, shall be required to make, alter, amend or repeal the by-laws of the Corporation; and (ii) to the full extent permitted or not prohibited by law, and without the consent of or other action by the stockholders, to authorize or create mortgages, pledges or other liens or encumbrances upon any or all of the assets, real, personal or mixed, and franchises of the Corporation, including after-acquired property, and to exercise all of the powers of the Corporation in connection therewith.

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ARTICLE EIGHT

Except as otherwise provided for by any resolutions of the Board of Directors providing for the issuance of any series of Preferred Stock, effective as of the IPO Closing, any action required or permitted to be taken by the stockholders of the Corporation may be taken only at a duly called annual or special meeting of the stockholders in which such action is properly brought before such meeting, and not by written consent in lieu of such a meeting. Subject to any special rights of the holders of any series of Preferred Stock, and to the requirements of applicable law, special meetings of stockholders of the Corporation may be called only by or at the direction of the Board of Directors pursuant to a resolution adopted by a majority of the total number of directors. Any business transacted at any special meeting of stockholders shall be limited to matters relating to the purpose or purposes stated in the notice of meeting

ARTICLE NINE

The Corporation reserves the right to amend, alter, change or repeal any provision contained in this Restated Certificate, in the manner now or hereafter prescribed by the DGCL, and all rights conferred upon stockholders herein are granted subject to this reservation. Notwithstanding anything to the contrary contained in this Restated Certificate, and notwithstanding that a lesser percentage may be permitted from time to time by applicable law, the affirmative vote of the holders of at least seventy-five percent (75%) of the outstanding shares of capital stock of the Corporation entitled to vote in the election of directors or class of directors, voting together as a single class (in addition to any separate class vote that may in the future be required pursuant to the terms of any outstanding Preferred Stock), shall be required to amend or repeal the provisions of Articles Four (only to the extent it relates to the authority of the Board of Directors to issue shares of Preferred Stock in one or more series, the terms of which may be determined by the Board of Directors), Six, Seven, Eight, Nine, Ten, or Eleven of this Restated Certificate or to reduce the numbers of authorized shares of Common Stock or Preferred Stock.

ARTICLE TEN

Section 1. Limitation of Liability. To the fullest extent permitted by the DGCL as it now exists or may hereafter be amended (but, in the case of any such amendment, only to the extent that such amendment permits the Corporation to provide broader indemnification rights than permitted prior thereto), no director of the Corporation shall be personally liable to the Corporation or to any of its stockholders for monetary damages for breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability; provided, however, that to the extent required from time to time by applicable law, this Article Ten shall not eliminate or limit the liability of a director, to the extent such liability is provided by applicable law, (i) for any breach of the director's duty of loyalty to the corporation or its stockholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under Section 174 of the DGCL, or (iv) for any transactions from which the director derived an improper personal benefit.

Section 2. Indemnification. The Corporation shall, to the fullest extent permitted by Section 145 of the DGCL and as further provided in the Corporation's by-laws, each as amended from time to time, indemnify each person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that such person is or was, or has agreed to become, a director or officer of the Corporation, or is or was serving, or has agreed to serve, at the request of the Corporation, as a director, officer or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees), judgments, fines and

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amounts paid in settlement actually and reasonably incurred by him or her or on his or her behalf in connection with such action, suit or proceeding and any appeal therefrom.

Indemnification may include payment by the Corporation of expenses in defending an action or proceeding in advance of the final disposition of such action or proceeding upon receipt of an undertaking by the person indemnified to repay such payment if it is ultimately determined that such person is not entitled to indemnification under this Article Ten, which undertaking may be accepted without reference to the financial ability of such person to make such repayment.

The Corporation shall not indemnify any such person seeking indemnification in connection with a proceeding (or part thereof) initiated by such person unless the initiation thereof was approved by the Board of Directors or except and to the extent otherwise permitted in the Corporation's by-laws or in an agreement between the Corporation and such person.

The indemnification rights provided in this Article Ten (i) shall not be deemed exclusive of any other rights to which those indemnified may be entitled under the Corporation's by-laws, any law, agreement or vote of stockholders or disinterested directors or otherwise, and (ii) shall inure to the benefit of the heirs, executors and administrators of such persons. The Corporation may, to the extent authorized from time to time by its Board of Directors, grant indemnification rights to other employees or agents of the Corporation or other persons serving the Corporation and such rights may be equivalent to, or greater or less than, those set forth in this Article Ten.

Section 3. Merger or Consolidation. For purposes of this Article Ten, references to the "Corporation" shall include, in addition to the resulting corporation, any constituent corporation (including any constituent of a constituent) absorbed in a consolidation or merger which, if its separate existence had continued, would have had power and authority to indemnify its directors, officers and employees or agents, so that any person who is or was a director, officer, employee or agent of such constituent corporation, or is or was serving at the request of such constituent corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, shall stand in the same position under this Article Ten with respect to the resulting or surviving corporation as he or she would have with respect to such constituent corporation if its separate existence had continued.

Section 4. Amendment or Repeal. No amendment to or repeal of this Article Ten shall apply to or have any effect on the liability or alleged liability of any director for or with respect to any acts or omissions of such director occurring prior to the effective date of such amendment or repeal.

ARTICLE ELEVEN

Unless the Corporation, as authorized by the Board of Directors, consents in writing to the selection of one or more alternative forums, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for a stockholder (including a beneficial owner) to bring (i) any derivative action or proceeding brought on behalf of the Corporation, (ii) any action asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee of the Corporation to the Corporation or the Corporation's stockholders, (iii) any action asserting a claim against the Corporation arising pursuant to any provision of the DGCL or this Restated Certificate or the Corporation's by-laws or (iv) any action asserting a claim against the Corporation, its directors, officers or employees governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of capital stock of the Corporation (including, without limitation, shares of Common Stock) shall, and shall be deemed to, have notice of and to have consented to the provisions of this Article Eleven.

ARTICLE TWELVE

If any provision or provisions of this Restated Certificate shall be held to be invalid, illegal or unenforceable as applied to any circumstance for any reason whatsoever: (i) the validity, legality and enforceability of such provisions in any other circumstance and of the remaining provisions of this Restated Certificate (including, without limitation, each portion of any paragraph of this Restated Certificate containing any such provision held to be invalid, illegal or unenforceable that is not itself held to be invalid, illegal or unenforceable) shall not in any way be affected or impaired thereby and (ii) to the fullest extent possible, the provisions of this Restated Certificate (including, without limitation, each such portion of any paragraph of this Restated Certificate containing any such provision held to be invalid, illegal or unenforceable) shall be construed so as to permit the Corporation to protect its directors, officers, employees and agents from personal liability in respect of their good faith service to or for the benefit of the Corporation to the fullest extent permitted by law.

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IN WITNESS WHEREOF, this Amended and Restated Certificate of Incorporation has been executed by a duly authorized officer of this Corporation on this day of , 2017.

RHYTHM PHARMACEUTICALS, INC.

By:

Name: Keith Gottesdiener
Title: Chief Executive Officer

[Signature Page to Amended and Restated Certificate of Incorporation of Rhythm Pharmaceuticals, Inc.]

**CERTIFICATE OF AMENDMENT
TO
AMENDED AND RESTATED CERTIFICATE OF INCORPORATION
OF
RHYTHM PHARMACEUTICALS, INC.**

Rhythm Pharmaceuticals, Inc. (the “Corporation”), a corporation organized and existing under and by virtue of the provisions of the General Corporation Law of the State of Delaware (the “General Corporation Law”), does hereby certify that:

1. The name of the corporation is Rhythm Pharmaceuticals, Inc., that the corporation was formerly known as Rhythm Metabolic, Inc., and the date the Corporation filed its original Certificate of Incorporation with the Secretary of State of the State of Delaware was February 26, 2013.
2. This Certificate of Amendment to the Certificate of Incorporation has been duly adopted in accordance with Sections 242 and 228 of the General Corporation Law by the directors and the stockholders of the Corporation. In lieu of a meeting and vote by the stockholders of the Corporation, the amendment certified herein has been duly adopted by written consent of the stockholders of the Corporation holding at least the minimum number of votes required to adopt said amendment, in accordance with the provisions of Section 228 of the General Corporation Law.
3. The Certificate of Incorporation is hereby amended by:

- (i) deleting the first paragraph of Article Fourth and replacing it with the following:

“FOURTH: The total number of shares of all classes of stock which the Corporation shall have authority to issue is (i) 29,919,979 shares of common stock, \$0.001 par value per share (“Common Stock”) and (ii) 159,616,209 shares of preferred stock, \$0.001 par value per share (“Preferred Stock”).

- (ii) Adding a paragraph after the first paragraph of Article Fourth which states:

“At the time of the filing of this Certificate of Amendment to the Certificate of Incorporation with the Office of the Secretary of State of Delaware (the “Effective Time”), a 1-for-9.17 reverse stock split of the issued and outstanding shares of the Common Stock of the Corporation shall become effective, whereby every nine and seventeen one-hundredth (9.17) shares of Common Stock issued and outstanding immediately prior to the Effective Time, automatically, and without any action on the part of the holder thereof, shall be reclassified into one (1) share of Common Stock (the “Reverse Stock Split”). No fractional shares of Common Stock shall be issued or issuable in connection with the Reverse Stock Split and, in lieu thereof, upon surrender after the Effective Time of a certificate which formerly represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time, any person who would otherwise be entitled to a fractional share of Common Stock as a result of the Reverse Stock Split, following the Effective Time, shall be entitled to receive a cash payment equal to the fraction of which such holder would otherwise be entitled multiplied by the fair value per share as determined by the board of directors.”

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4. This Certificate of Incorporation, as amended, is hereby ratified and confirmed in all other respects.

[The remainder of this page intentionally left blank]

IN WITNESS WHEREOF, the undersigned has caused this Certificate of Amendment to the Certificate of Incorporation to be duly executed on behalf of the Corporation on _____, 2017.

RHYTHM PHARMACEUTICALS, INC.

By:

Name: Keith Gottesdiener

Title: Chief Executive Officer

[Rhythm Pharmaceuticals, Inc. – Signature Page to Amendment to Certificate of Incorporation]

RHYTHM PHARMACEUTICALS, INC.

AMENDED AND RESTATED BYLAWS

Article I. — General.

1.1. Offices. The registered office of Rhythm Pharmaceuticals, Inc. (the “Company”) shall be in the City of Wilmington, County of New Castle, State of Delaware. The Company may also have offices at such other places both within and without the State of Delaware as the board of directors of the Company (the “Board of Directors”) may from time to time determine or the business of the Company may require.

1.2. Seal. The seal, if any, of the Company shall be in the form of a circle and shall have inscribed thereon the name of the Company, the year of its organization and the words “Corporate Seal, Delaware.”

1.3. Fiscal Year. The fiscal year of the Company shall be fixed by resolution of the Board of Directors.

Article II. — Stockholders.

2.1. Place of Meetings. Each meeting of the stockholders shall be held upon notice as hereinafter provided, at such place as the Board of Directors shall have determined and as shall be stated in such notice, either within or outside the State of Delaware.

2.2. Annual Meeting. The annual meeting of the stockholders shall be held each year on such date and at such time as the Board of Directors may determine. At each annual meeting the stockholders entitled to vote shall elect such members of the Board of Directors as are standing for election, by plurality vote by ballot, and they may transact such other corporate business as may properly be brought before the meeting. At the annual meeting any business may be transacted, irrespective of whether the notice calling such meeting shall have contained a reference thereto, except where notice is required by law, the Company’s Amended and Restated Certificate of Incorporation (as amended from time to time, the “Company’s Certificate of Incorporation”), or these By-laws.

2.3. Quorum and Adjournment. At all meetings of the stockholders the holders of a majority of the stock issued and outstanding and entitled to vote thereat, present in person or represented by proxy, shall constitute a quorum requisite for the transaction of business except as otherwise provided by law, the Company’s Certificate of Incorporation, or these By-laws. Whether or not there is such a quorum at any meeting, the presiding officer of the meeting may adjourn the meeting from time to time without notice other than announcement at the meeting. If the adjournment is for more than thirty (30) days, or if after the adjournment a new record date is fixed for the adjourned meeting, a notice of the adjourned meeting shall be given to each stockholder of record entitled to vote at the meeting. At such adjourned meeting, at which the requisite amount of voting stock shall be represented, any business may be transacted that might have been transacted if the meeting had been held as originally called. The stockholders present in person or by proxy at a duly called meeting at which a quorum is present may continue to transact business until adjournment, notwithstanding the withdrawal of enough stockholders to leave less than a quorum.

2.4. Right to Vote; Proxies. Subject to the provisions of the Company’s Certificate of Incorporation, each holder of a share or shares of capital stock of the Company having the right to vote at any meeting shall be entitled to one vote for each such share of stock held by such stockholder. Any

stockholder entitled to vote at any meeting of stockholders may vote either in person or by proxy, but no proxy that is dated more than three (3) years prior to the meeting at which it is offered shall confer the right to vote thereat unless the proxy provides that it shall be effective for a longer period. A proxy may be granted by a writing executed by the stockholder or his or her authorized agent or by transmission or authorization of transmission by means of electronic transmission to the person who will be the holder of the proxy or to a proxy solicitation firm, proxy support service organization, or like agent duly authorized by the person who will be the holder of the proxy to receive such transmission, subject to the conditions set forth in Section 212 of the Delaware General Corporation Law, as it may be amended from time to time (the “DGCL”).

2.5. Voting. At all meetings of stockholders, except as otherwise expressly provided for by statute, the Company’s Certificate of Incorporation, or these By-laws, (i) in all matters other than the election of directors, the affirmative vote of a majority of shares present in person or represented by proxy at the meeting and entitled to vote on such matter shall be the act of the stockholders, and (ii) directors shall be elected by a plurality of the votes cast, present in person or represented by proxy at the meeting and entitled to vote on the election of directors.

2.6. Notice of Annual Meetings. Written notice of the annual meeting of the stockholders shall be mailed to each stockholder of record entitled to vote thereat at such address as appears on the stock books of the Company at least ten (10) days (and not more than sixty (60) days) prior to the meeting. The Board of Directors may postpone any annual meeting of the stockholders at its discretion, even after notice thereof has been mailed. It shall be the duty of every stockholder to furnish to the Secretary of the Company or to the transfer agent, if any, of the class of stock owned by him or her, such stockholder’s post-office address, and to notify the Secretary of any change therein. Notice need not be given to any stockholder who submits a written waiver of notice signed by him or her before or after the time stated therein. Attendance of a stockholder at a meeting of stockholders shall constitute a waiver of notice of such meeting, except when the stockholder attends the meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Neither the business to be transacted at, nor the purpose of, any regular or special meeting of the stockholders need be specified in any written waiver of notice.

2.7. Stockholders’ List. A complete list of the stockholders entitled to vote at any meeting of stockholders, arranged in alphabetical order and showing the address of each stockholder, and the number of shares registered in the name of each stockholder, shall be prepared by the Secretary and shall be open to the examination of any stockholder, for any purpose germane to the meeting for a period of at least ten (10) days before such meeting (i) on a reasonably accessible electronic network, provided that the information required to gain access to such list is provided with the notice of the meeting, or (ii) during ordinary business hours, at the principal place of business of the Company, and said list shall be produced and kept at the time and place of such meeting during the whole time of said meeting, and may be inspected by any stockholder who is present at the place of said meeting, or, if the meeting is to be held solely by means of remote communication, on a reasonably accessible electronic network and the information required to access such list shall be provided with the notice of the meeting.

2.8. Special Meetings. Special meetings of the stockholders for any purpose or purposes, unless otherwise provided by law, may be called only in the manner set forth in the Company's Certificate of Incorporation. Any such person or persons that has or have called a special meeting of stockholders in the manner set forth in the Company's Certificate of Incorporation may postpone or cancel any special meeting of the stockholders at its or their discretion, even after notice thereof has been mailed.

2.9. Notice of Special Meetings. Written notice of a special meeting of stockholders, stating the time and place and purpose or purposes thereof, shall be mailed, postage prepaid, not less than ten (10) nor more than sixty (60) days before such meeting, to each stockholder of record entitled to vote thereat, at such address as appears on the books of the Company. No business may be transacted at such meeting except that referred to in said notice, or in a supplemental notice given also in compliance with the provisions hereof, or such other business as may be germane or supplementary to that stated in said notice or notices. The individual or group calling such meeting shall have exclusive authority to determine the business included in such notice. Notice need not be given to any stockholder who submits a written waiver of notice signed by him or her before or after the time stated therein. Attendance of a stockholder at a meeting of stockholders shall constitute a waiver of notice of such meeting, except when the stockholder attends the meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Neither the business to be transacted at, nor the purpose of, any regular or special meeting of the stockholders need be specified in any written waiver of notice.

2.10. Inspectors of Elections; Opening and Closing the Polls.

(a) One or more inspectors may be appointed by the Board of Directors before or at any meeting of stockholders, or, if no such appointment shall have been made, the presiding officer may make such appointment at the meeting. At the meeting for which the inspector or inspectors are appointed, he, she or they shall open and close the polls, receive and take charge of the proxies and ballots, and decide all questions touching on the qualifications of voters, the validity of proxies, and the acceptance and rejection of votes. If any inspector previously appointed shall fail to attend or refuse or be unable to serve, the presiding officer shall appoint an inspector in his or her place.

(b) At any time at which the Company has a class of voting stock that is (i) listed on a national securities exchange, (ii) authorized for quotation on an inter-dealer quotation system of a registered national securities association, or (iii) held of record by more than 2,000 stockholders, the provisions of Section 231 of the DGCL with respect to inspectors of election and voting procedures shall apply, in lieu of the provisions of paragraph (a) of this Section 2.10.

2.11. Stockholders' Consent in Lieu of Meeting. Unless otherwise provided in the Company's Certificate of Incorporation, any action required to be taken at any annual or special meeting of stockholders of the Company, or any action that may be taken at any annual or special meeting of such stockholders, may be taken only at such a meeting, and not by written consent of the stockholders.

2.12. Advance Notice of Stockholder Business and Nominations.

(a) Timely Notice. At a meeting of the stockholders, only such nominations of persons for the election of directors and such other business shall be conducted as shall have been properly brought before the meeting. To be properly brought before an annual meeting, nominations or such other business must be: (i) specified in the notice of meeting (or any supplement thereto) given by or at the direction of the Board of Directors or any committee thereof, (ii) otherwise properly brought before the meeting by or at the direction of the Board of Directors or any committee thereof, or (iii) otherwise properly brought before the meeting by a stockholder who is a stockholder of record or beneficial owner of shares of the Company's capital stock at the time such notice of meeting is delivered, who is entitled to vote at the meeting and who complies with the notice procedures set forth in this Section 2.12. In addition, any proposal of business (other than the nomination of persons for election to the Board of Directors) must be a proper matter for stockholder action. For business (including, but not limited to, director nominations) to be properly brought before an annual meeting by a stockholder, the Proposing Stockholder (as defined below) must have given timely and proper notice thereof pursuant to this Section 2.12, in writing to the

Secretary of the Company even if such matter is already the subject of any notice to the stockholders or a disclosure made in a press release reported by the Dow Jones News Services, The Associated Press or a comparable national news service or in a document filed by the Company with the Securities and Exchange Commission pursuant to Section 13, 14 or 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act") from the Board of Directors (a "Public Disclosure"). For purposes of these By-laws, Proposing Stockholder means (i) the stockholder providing the notice of proposed business or director nomination, (ii) the beneficial owner of the Company's capital stock, if different, on whose behalf the proposed business or director nomination, as applicable, is given, (iii) any affiliate or associate (as defined under the Exchange Act) of such stockholder or beneficial owner, (iv) each person who is a member of a "group" (for purposes of these By-laws, as such term is used in Rule 13d-5 under the Exchange Act) with any such stockholder or beneficial owner (or their respective affiliates and associates) or is otherwise Acting in Concert (as defined below) with any such stockholder or beneficial owner (or their respective affiliates and associates) with respect to the proposals or proposed nominations, as applicable, and (v) any participant (as defined in paragraphs (a)(ii)-(vi) of Instruction 3 to Item 4 of Schedule 14A, or any successor instructions) with such stockholder or beneficial owner in the solicitation of proxies in respect of any proposed nominations or other business proposed to be brought before the Company's stockholders. To be timely, a Proposing Stockholder's notice must be delivered to or mailed and received at the principal executive offices of the Company: (x) not later than the close of business on the ninetieth (90th) calendar day, nor earlier than the close of business on the one hundred twentieth (120th) calendar day in advance of the anniversary of the previous year's annual meeting if such meeting is to be held on a day which is not more than thirty (30) calendar days in advance of the anniversary of the previous year's annual meeting or not later than sixty (60) calendar days after the anniversary of the previous year's annual meeting; and (y) with respect to any other annual meeting of stockholders, the close of business on the tenth (10th) calendar day following the date of Public Disclosure of the date of such meeting. In no event shall the Public Disclosure of an adjournment or postponement of an annual meeting commence a new notice time period (or extend any notice time period). For purposes of these By-laws, "close of business" shall mean 5:00 p.m. local time at the principal executive offices of the Company on any calendar day, whether or not such day is a business day.

(b) Stockholder Nominations. For the nomination of any person or persons for election to the Board of Directors, a Proposing Stockholder's notice to the Secretary of the Company shall set forth (i) the name, age, business address and residence address of each nominee proposed in such notice, (ii) the principal occupation or employment of each such nominee, (iii) the number of shares of capital stock of the Company which are owned of record and

beneficially by each such nominee (if any), (iv) such other information concerning each such nominee as would be required to be disclosed in a proxy statement soliciting proxies for the election of such nominee as a director in an election contest (even if an election contest is not involved) or that is otherwise required to be disclosed, under Section 14(a) of the Exchange Act and the rules and regulations promulgated thereunder, (v) the consent of the nominee to being named in the proxy statement as a nominee and to serving as a director if elected, and (vi) as to the Proposing Stockholder: (A) the name and address of the Proposing Stockholder as they appear on the Company's books and of the beneficial owner, if any, on whose behalf the nomination is being made, (B) the class and number of shares of the Company which are owned by the Proposing Stockholder (beneficially and of record) and owned by the beneficial owner, if any, on whose behalf the nomination is being made, as of the date of the Proposing Stockholder's notice, and a representation that the Proposing Stockholder will notify the Company in writing of the class and number of such shares owned of record and beneficially as of the record date for the meeting promptly following the later of the record date or the date notice of the record date is first publicly disclosed, (C) a description of any agreement, arrangement or understanding with respect to such nomination between or among the Proposing Stockholder and the beneficial owner, if any, on whose behalf the nomination is being made, and any of their affiliates or associates, and any others (including their names) Acting in Concert with any of the foregoing, and a representation that the Proposing Stockholder will notify the Company in writing of any such agreement,

arrangement or understanding in effect as of the record date for the meeting promptly following the later of the record date or the date notice of the record date is first publicly disclosed, (D) a description of any agreement, arrangement or understanding (including any derivative or short positions, profit interests, options, hedging transactions, and borrowed or loaned shares) that has been entered into as of the date of the Proposing Stockholder's notice by, or on behalf of, the Proposing Stockholder or any of its affiliates or associates, the effect or intent of which is to mitigate loss to, manage risk or benefit of share price changes for, or increase or decrease the voting power of the Proposing Stockholder, or any such beneficial owner, or any of its affiliates or associates with respect to shares of stock of the Company, and a representation that the Proposing Stockholder will notify the Company in writing of any such agreement, arrangement or understanding in effect as of the record date for the meeting promptly following the later of the record date or the date notice of the record date is first publicly disclosed, (E) a representation that the Proposing Stockholder is a holder of record of shares of the Company entitled to vote at the meeting and intends to appear in person or by proxy at the meeting to nominate the person or persons specified in the notice, (F) a representation as to whether the Proposing Stockholder intends to deliver a proxy statement and/or form of proxy to holders of at least the percentage of the Company's outstanding capital stock required to approve the nomination and/or otherwise to solicit proxies from stockholders in support of the nomination, (G) the full notional amount of any securities that, directly or indirectly, underlie any "derivative security" (as such term is defined in Rule 16a-1(c) under the Exchange Act) that constitutes a "call equivalent position" (as such term is defined in Rule 16a-1(b) under the Exchange Act) (together, a "Synthetic Equity Position") and that is, directly or indirectly, held or maintained by such Proposing Stockholder with respect to any shares of any class or series of shares of the Company; *provided that*, for the purposes of the definition of "Synthetic Equity Position," the term "derivative security" shall also include any security or instrument that would not otherwise constitute a "derivative security" (as such term is defined in Rule 16a-1(c) under the Exchange Act) as a result of any feature that would make any conversion, exercise or similar right or privilege of such security or instrument becoming determinable only at some future date or upon the happening of a future occurrence, in which case the determination of the amount of securities into which such security or instrument would be convertible or exercisable shall be made assuming that such security or instrument is immediately convertible or exercisable at the time of such determination; and, *provided, further*, that any Proposing Stockholder satisfying the requirements of Rule 13d-1(b)(1) under the Exchange Act (other than a Proposing Stockholder that so satisfies Rule 13d-1(b)(1) under the Exchange Act solely by reason of Rule 13d-1(b)(1)(ii)(E)) shall not be deemed to hold or maintain the notional amount of any securities that underlie a Synthetic Equity Position held by such Proposing Stockholder as a hedge with respect to a bona fide derivatives trade or position of such Proposing Stockholder arising in the ordinary course of such Proposing Stockholder's business as a derivatives dealer and (H) all other information relating to such Proposing Stockholder that would be required to be disclosed in a proxy statement or other filing if such a filing was to be made by any Proposing Stockholder in connection with the contested solicitation of proxies or consents (even if a contested solicitation is not involved) by any Proposing Stockholder in support of the business or nomination proposed to be brought before the meeting pursuant to this Section 2.12 and Regulation 14A under the Exchange Act. The Company may require any proposed nominee to furnish such other information as it may reasonably require to determine the eligibility of such proposed nominee to serve as an independent director of the Company or that could be material to a reasonable stockholder's understanding of the independence, or lack thereof, of such nominee. For purposes of these By-laws, a person shall be deemed to be "Acting in Concert" with another person if such person knowingly acts (whether or not pursuant to an express agreement, arrangement or understanding) in concert with, or towards a common goal relating to the management, governance or control of the Company in parallel with, such other person where (A) each person is conscious of the other person's conduct or intent and this awareness is an element in their decision-making processes and (B) at least one additional factor suggests that such persons intend to act in concert or in parallel, which such additional factors may include, without limitation, exchanging information (whether publicly or privately), attending meetings, conducting discussions, or making or soliciting invitations to act in concert or in parallel; provided,

however, that a person shall not be deemed to be Acting in Concert with any other person solely as a result of the solicitation or receipt of revocable proxies, or special meeting demands from such other person in response to a solicitation made pursuant to, and in accordance with, Section 14(a) of the Exchange Act by way of a proxy statement filed on Schedule 14A. A person deemed to be Acting in Concert with another person shall be deemed to be Acting in Concert with any third party who is also Acting in Concert with such other person.

(c) Other Stockholder Proposals. For all business other than director nominations, a Proposing Stockholder's notice to the Secretary of the Company shall set forth as to each matter the Proposing Stockholder proposes to bring before the annual meeting: (i) a brief description of the business desired to be brought before the annual meeting and the reasons for conducting such business at the annual meeting, (ii) the text of the proposal or business (including the text of any resolutions proposed for consideration), (iii) a description in reasonable detail of any interest of any Proposing Stockholder in such business, including any anticipated benefit to the stockholder or any other Proposing Stockholder therefrom, including any interest that will be disclosed to the Company's stockholders in any proxy statement to be distributed to the Company's stockholders, (iv) any other information relating to such stockholder and beneficial owner, if any, on whose behalf the proposal is being made, required to be disclosed in a proxy statement or other filings required to be made in connection with solicitations of proxies for the proposal and pursuant to and in accordance with Section 14(a) of the Exchange Act and the rules and regulations promulgated thereunder and (v) the information required by Section 2.12(b)(vi) above.

(d) Proxy Rules. In addition to the provisions of this Section 2.12, a Proposing Stockholder shall also comply with all applicable requirements of the Exchange Act and the rules and regulations promulgated thereunder, the DGCL, and other applicable law with respect to any nominations of directors for election at any stockholders' meeting and any business that may be brought before any stockholders' meeting and any solicitations of proxies in connection therewith and any filings required to be made with the SEC in connection therewith. Nothing in this Section 2.12 shall be deemed to affect any

rights of stockholders to request inclusion of proposals in the Company's proxy statement pursuant to Rule 14a-8 under the Exchange Act or any other rights conferred on stockholders by a rule under the Exchange Act.

(e) Notwithstanding anything to the contrary contained in this Section 2.12, the information required to be included in a Proposing Stockholder's notice of business or director nomination shall not include any ordinary course business activities of any broker, dealer, commercial bank, trust company or other nominee who, in the ordinary course of business, is directed to prepare and submit such notice on behalf of a beneficial owner of the shares held of record by such broker, dealer, commercial bank, trust company or other nominee and who is not otherwise affiliated or associated with such beneficial owner.

(f) Updating of Notice of Proposed Business or Director Nomination.

(i) A stockholder providing notice of any business proposed to be conducted at an annual meeting or notice of a director nomination shall further update and supplement such notice, as necessary, from time to time, so that the information provided or required to be provided in such notice pursuant to Sections 2.12(b) and 2.12(c) shall be true, correct and complete in all respects not only prior to the deadline for submitting such notice but also at all times thereafter and prior to the annual meeting, and such update and supplement shall be received by the Secretary of the Company not later than the earlier of (A) five (5) business days following the occurrence of any event, development or occurrence which would cause the information provided to be not true, correct and complete in all respects, and (B) ten (10) business days prior to the meeting at which such proposals or nominations contained therein are to be considered.

(ii) If the information submitted pursuant to Section 2.12(b) or 2.12(c) by any stockholder proposing business for consideration at an annual meeting or a director nomination shall not be true, correct and complete in all respects prior to the deadline for submitting such notice, such information may be deemed not to have been provided in accordance with this Section 2.12. For the avoidance of doubt, the updates required pursuant to this Section 2.12 do not cause a notice that was not in compliance with this Section 2.12 when first delivered to the Company prior to the deadline for submitting such notice to thereafter be in proper form in accordance with this Section 2.12.

(iii) Upon written request by the Secretary of the Company, the Board of Directors (or any duly authorized committee thereof), any stockholder submitting a notice proposing business for consideration at an annual meeting or a director nomination shall provide, within five (5) business days of delivery of such request (or such other period as may be specified in such request), written verification, satisfactory in the reasonable discretion of the Board of Directors, any duly authorized committee thereof or any duly authorized officer of the Company, to demonstrate the accuracy of any information submitted by the stockholder in such notice delivered pursuant to this Section 2.12 (including, if requested by the Company, written confirmation by such stockholder that it continues to intend to bring the business proposed or director nomination referenced in the notice before the meeting). If a stockholder fails to provide such written verification within such period, the information as to which written verification was requested may be deemed not to have been provided in accordance with this Section 2.

(g) Referencing and Cross-Referencing. For a notice proposing business or a director nomination at a stockholders' meeting to comply with the requirements of Sections 2.12(b) and 2.12(c), each of the requirements of Sections 2.12(b) and 2.12(c) shall be directly and expressly responded to and a notice must clearly indicate and expressly reference which provisions of Sections 2.12(b) and 2.12(c) the information disclosed is intended to be responsive to. Information disclosed in one section of a notice in response to one provision of Sections 2.12(b) or 2.12(c) shall not be deemed responsive to any other provision of Sections 2.12(b) or 2.12(c) unless it is expressly cross-referenced to such other provision and it is clearly apparent how the information included in one section of the notice is directly and expressly responsive to the information required to be included in another section of the notice pursuant to Sections 2.12(b) or 2.12(c). For the avoidance of doubt, statements purporting to provide global cross-references that purport to provide that all information provided shall be deemed to be responsive to all requirements of Sections 2.12(b) and 2.12(c) shall not satisfy the requirements of this paragraph (g) of this Section 2.12.

(h) No Incorporation by Reference. For a notice proposing business or a director nomination at a stockholders' meeting to comply with the requirements of Sections 2.12(b) and 2.12(c), it must set forth in writing directly within the body of the notice (as opposed to being incorporated by reference from any other document or writing not prepared in response to the requirements of this Section 2.12) all the information required to be included therein as set forth in Sections 2.12(b) and 2.12(c) and each of the requirements of Sections 2.12(b) and 2.12(c) shall be directly responded to in a manner that makes it clearly apparent how the information provided is specifically responsive to any requirements of Sections 2.12(b) and 2.12(c). For the avoidance of doubt, a notice shall not be deemed to be in compliance with Section 2.12 if it attempts to include the required information by incorporating by reference into the body of the notice any other document, writing or part thereof, including, but not limited to, any documents publicly filed with the U.S. Securities and Exchange Commission. For the further avoidance of doubt, the body of the notice does not include any documents not prepared in response to the requirements of this Section 2.12.

(i) Accuracy of Information. A stockholder submitting a notice of proposed business or director nomination, by its delivery to the Company, represents and warrants that all information

contained therein, as of the deadline for submitting such notice, is true, accurate and complete in all respects, contains no false and misleading statements and such stockholder acknowledges that it intends for the Company and the Board of Directors to rely on such information as (i) being true, accurate and complete in all respects and (ii) not containing any false or misleading statements.

(j) Special Meetings of Stockholders. Only such business shall be conducted at a special meeting of stockholders as shall have been brought before the meeting pursuant to the Company's notice of meeting. Nominations of persons for election to the Board of Directors may be made at a special meeting of stockholders at which directors are to be elected pursuant to the Company's notice of meeting (x) by or at the direction of the Board of Directors or any committee thereof or (y) provided that the Board of Directors has determined that directors shall be elected at such meeting, by any stockholder of the Company who is a beneficial owner or stockholder of record at the time the notice provided for in this Section 2.12 is delivered to the Secretary of the Company, who is entitled to vote at the meeting and upon such election and who complies with the notice procedures set forth in this Section 2.12. In the event the Company calls a special meeting of stockholders for the purpose of electing one or more directors to the Board of Directors, any such stockholder

entitled to vote in such election of directors may nominate a person or persons (as the case may be) for election to such position(s) as specified in the Company's notice of meeting, if the stockholder's notice required by this Section 2.12 shall be delivered to the Secretary at the principal executive offices of the Company not later than the later of the close of business on the ninetieth (90th) day prior to such special meeting or the tenth (10th) day following the date of Public Disclosure of the date of the special meeting and of the nominees proposed by the Board of Directors to be elected at such meeting and not earlier than the close of business on the one hundred twentieth (120th) day prior to such special meeting. In no event shall the Public Disclosure of an adjournment or postponement of a special meeting commence a new time period (or extend any notice time period).

(k) **Effect of Noncompliance.** Notwithstanding anything in these By-laws to the contrary, (i) no nominations shall be made or business shall be conducted at any annual meeting except in accordance with the procedures set forth in this Section 2.12, and (ii) unless otherwise required by law, if a Proposing Stockholder intending to propose business or make nominations at an annual meeting pursuant to this Section 2.12 does not provide the information required under this Section 2.12 to the Company promptly following the later of the record date or the date notice of the record date is first publicly disclosed, or the Proposing Stockholder (or a qualified representative of the Proposing Stockholder) does not appear at the meeting to present the proposed business or nominations, such business or nominations shall not be considered, notwithstanding that proxies in respect of such business or nominations may have been received by the Company. For purposes of these By-laws, "qualified representative" means (i) if the stockholder is a corporation, any duly authorized officer of such corporation, (ii) if the stockholder is a limited liability company, any duly authorized member, manager or officer of such limited liability company, (iii) if the stockholder is a partnership, any general partner or person who functions as general partner for such partnership, (iv) if the stockholder is a trust, the trustee of such trust, or (v) if the stockholder is an entity other than the foregoing, the persons acting in such similar capacities as the foregoing with respect to such entity.

Article III. — Directors.

3.1. Number of Directors.

(a) Except as otherwise provided by law, the Company's Certificate of Incorporation, or these By-laws, the property and business of the Company shall be managed by or under the direction of the Board of Directors. Directors need not be stockholders, residents of Delaware, or citizens of the

United States. The use of the phrase "whole board" herein refers to the total number of directors which the Company would have if there were no vacancies.

(b) Subject to the special rights of the holders of any series of Preferred Stock to elect directors, the number of directors constituting the full Board of Directors shall be as determined by the Board of Directors from time to time by resolution adopted by the affirmative vote of at least a majority of the directors then in office.

(c) Effective as of the closing (the "IPO Closing") of the Company's first public offering of shares of Common Stock registered pursuant to the Securities Act of 1933, as amended, the Board of Directors shall be divided into three classes of directors, such classes to be as nearly equal in number of directors as possible, having staggered three-year terms of office (except to the extent otherwise provided in the next sentence with respect to the initial term of such classes of directors). The initial term of office of the directors of the first such class shall expire as of the first annual meeting of the Company's stockholders following the IPO Closing; the initial term of office of the directors of the second such class shall expire as of the second annual meeting of the Company's stockholders following the IPO Closing; and the initial term of office of the directors of the third such class shall expire as of the third annual meeting of the Company's stockholders following the IPO Closing. At each annual meeting of stockholders of the Company after the IPO Closing, nominees will stand for election to succeed those directors whose terms are to expire as of such annual meeting of stockholders, and such nominees elected at such annual meeting of stockholders shall be elected for a term expiring at the third annual meeting of stockholders following their election.

(d) Directors shall hold office until the annual meeting of stockholders in which their term is scheduled to expire as set forth above in this Section 3.1 and until their respective successors are duly elected or qualified or until their earlier death, incapacity, resignation or removal. Any director serving as such pursuant to this Section 3.1 may be removed pursuant to Section 3.3. Those directors already in office immediately prior to the IPO Closing shall be allocated among the three (3) classes of directors contemplated under this Section 3.1 pursuant to a resolution or resolutions adopted by the Board of Directors prior to the IPO Closing.

(e) Except as the DGCL or the Company's Certificate of Incorporation may otherwise require, any new directorships or vacancies in the Board of Directors, including new directorships resulting from any increase in the number of directors to serve on the whole board and/or any unfilled vacancies by reason of death, resignation, disqualification, removal for cause, failure to elect or otherwise with respect to any director, may be filled by only the vote of a majority of the remaining directors then in office, although less than a quorum, or by the sole remaining director.

(f) No decrease in the number of directors constituting the whole board shall shorten the term of any incumbent director.

3.2. Resignation. Any director of the Company may resign at any time by giving notice in writing or by electronic transmission to the Chairperson of the Board, the President, or the Secretary of the Company. Such resignation shall take effect at the time specified therein, at the time of receipt if no time is specified therein and at the time of acceptance if the effectiveness of such resignation is conditioned upon its acceptance. Unless otherwise specified therein, the acceptance of such resignation shall not be necessary to make it effective.

3.3. Removal. Except as may otherwise be provided by the DGCL or the Company's Certificate of Incorporation, any director or the entire Board of Directors may be removed only for cause and only by the vote of the holders of at least seventy-five percent (75%) of the outstanding shares of

capital stock of the Company entitled to vote for the election of directors or class of directors, voting together as single class, at a meeting of the stockholders called for that purpose.

3.4. Place of Meetings and Books. The Board of Directors may hold their meetings and keep the books of the Company outside the State of Delaware, at such places as they may from time to time determine.

3.5. General Powers. In addition to the powers and authority expressly conferred upon them by these By-laws, the Board of Directors may exercise all such powers of the Company and do all such lawful acts and things as are not by statute or by the Company's Certificate of Incorporation or by these By-laws directed or required to be exercised or done by the stockholders.

3.6. Committees. The Board of Directors may designate one or more committees, by resolution or resolutions passed by at least a majority vote of the Board of Directors; such committee or committees shall consist of one or more directors of the Company, and to the extent provided in the resolution or resolutions designating them, shall have and may exercise specific powers of the Board of Directors in the management of the business and affairs of the Company to the extent permitted by statute and shall have power to authorize the seal of the Company to be affixed to all papers that may require it. Such committee or committees shall have such name or names as may be determined from time to time by resolution adopted by the Board of Directors.

3.7. Powers Denied to Committees. Committees of the Board of Directors shall not, in any event, have any power or authority to amend the Company's Certificate of Incorporation (except that a committee may, to the extent authorized in the resolution or resolutions providing for the issuance of shares adopted by the Board of Directors as provided in Section 151(a) of the DGCL, fix the designations and any of the preferences or rights of such shares relating to dividends, redemption, dissolution, any distribution of assets of the Company or the conversion into, or the exchange of such shares for, shares of any other class or classes or any other series of the same or any other class or classes of stock of the Company or fix the number of shares of any series of stock or authorize the increase or decrease of the shares of any series), adopt an agreement of merger or consolidation, recommend to the stockholders the sale, lease, or exchange of all or substantially all of the Company's property and assets, recommend to the stockholders a dissolution of the Company or a revocation of a dissolution, or amend the By-laws of the Company. Further, no committee of the Board of Directors shall have the power or authority to declare a dividend, to authorize the issuance of stock, or to adopt a certificate of ownership and merger pursuant to Section 253 of the DGCL, unless the resolution or resolutions designating such committee expressly so provides.

3.8. Substitute Committee Member. In the absence or on the disqualification of a member of a committee, the member or members thereof present at any meeting and not disqualified from voting, whether or not he, she or they constitute a quorum, may unanimously appoint another member of the Board of Director's to act at the meeting in the place of such absent or disqualified member. Any committee shall keep regular minutes of its proceedings and report the same to the Board of Directors as may be required by the Board of Directors.

3.9. Compensation of Directors. The Board of Directors shall have the power to fix the compensation of directors and members of committees of the Board. The directors may be paid their expenses, if any, of attendance at each meeting of the Board of Directors and may be paid a fixed sum for attendance at each meeting of the Board of Directors, a stated amount per annum as director and/or other forms of compensation as the Board of Directors may approve. No such payment shall preclude any director from serving the Company in any other capacity and receiving compensation therefor. Members of special or standing committees may be allowed like compensation for attending committee meetings.

3.10. Regular Meetings. No notice shall be required for regular meetings of the Board of Directors for which the time and place have been fixed.

3.11. Special Meetings. Special meetings of the Board of Directors may be called by the Chairperson of the Board of Directors, if any, or the Chief Executive Officer, on two (2) days' notice, which may be written, oral or by electronic transmission, to each director, or such shorter period of time before the meeting as will nonetheless be sufficient for the convenient assembly of the directors so notified; special meetings shall be called by the Secretary in like manner and on like notice, on the written request of two (2) or more directors.

3.12. Quorum. At all meetings of the Board of Directors, a majority of the members of the Board of Directors shall be necessary and sufficient to constitute a quorum for the transaction of business, and the act of a majority of the directors present at any meeting at which there is a quorum shall be the act of the Board of Directors, except as may be otherwise specifically permitted or provided by statute, by the Company's Certificate of Incorporation, or by these By-laws. If at any meeting of the Board of Directors there shall be less than a quorum present, a majority of those present may adjourn the meeting from time to time until a quorum is obtained, and no further notice thereof need be given other than by announcement at said meeting that shall be so adjourned.

3.13. Telephonic Participation in Meetings. Members of the Board of Directors or any committee designated by the Board of Directors may participate in a meeting of the Board of Directors or committee by means of conference telephone or similar communications equipment by means of which all persons participating in the meeting can hear one another, and participation in a meeting pursuant to this section shall constitute presence in person at such meeting.

3.14. Action by Consent. Unless otherwise restricted by the Company's Certificate of Incorporation or these By-laws, any action required or permitted to be taken at any meeting of the Board of Directors or of any committee thereof may be taken without a meeting, if written consent thereto is signed or submitted by electronic transmission by all members of the Board of Directors or of such committee as the case may be, and such written consent is filed with the minutes of proceedings of the Board of Directors or committee.

3.15. Chairperson of the Board. The Board of Directors may elect or remove, by the affirmative vote of at least a majority of the directors then in office, a Chairperson. Any Chairperson must be a director of the Company. The Chairperson shall preside at all meetings of the Board of Directors and at all meetings of the stockholders and, subject to the provisions of these By-laws and the direction of the Board of Directors, the Chairperson shall have such powers and perform such duties that are commonly incident to the position of chairperson of the board or as may be prescribed from time to time by the Board of Directors or provided in these By-laws.

Article IV. — Officers.

4.1. Selection; Statutory Officers. The officers of the Company shall be chosen by the Board of Directors. There shall be a President, a Secretary, and a Treasurer, and there may be a Chairperson of the Board of Directors, a Chief Executive Officer, one or more Vice Presidents, one or more Assistant Secretaries, and one or more Assistant Treasurers, as the Board of Directors may elect. Any number of offices may be held by the same person.

4.2. Time of Election. The officers above named shall be chosen by the Board of Directors at its first meeting after each annual meeting of stockholders. Other than the Chairperson, none of said officers need be a director.

4.3. Additional Officers. The Board of Directors may appoint such other officers and agents as it shall deem necessary, who shall hold their offices for such terms and shall exercise such powers and perform such duties as shall be determined from time to time by the Board of Directors.

4.4. Terms of Office. Each officer of the Company shall hold office until such officer's successor is chosen and qualified, or until such officer's earlier death, resignation or removal. Any officer may be removed at any time by the Board of Directors.

4.5. Compensation of Officers. The Board of Directors shall have power to fix the compensation of all officers of the Company. It may authorize any officer, upon whom the power of appointing subordinate officers may have been conferred, to fix the compensation of such subordinate officers.

4.6. Chief Executive Officer. The Chief Executive Officer, if any, in the absence or disability of the Chairperson of the Board, shall preside at all meetings of the stockholders, shall have general and active management of the business of the Company, and shall see that all orders and resolutions of the Board of Directors are carried into effect. The Chief Executive Officer shall execute bonds, mortgages, and other contracts requiring a seal, under the seal of the Company, except where required or permitted by law to be otherwise signed and executed and except where the signing and execution thereof shall be expressly delegated by the Board of Directors to some other officer or agent of the Company. In the absence of the Chief Executive Officer, the President, the Chairperson, or another officer of the Company, as designated by the Board of Directors, shall have the powers of the Chief Executive Officer.

4.7. President and Vice-Presidents. The President shall act in an executive capacity as shall be directed from time to time by the Board of Directors or the Chief Executive Officer, and shall have such powers and perform such other duties as the Board of Directors or the Chief Executive Officer may determine from time to time (which may include, without limitation, assisting the Chief Executive Officer in the operation and administration of the Company's business and the supervision of its policies and affairs), with such limitations on such powers or performance of duties as either of the foregoing shall prescribe. The Vice-President, or if there shall be more than one, the Vice-Presidents in the order determined by the Board of Directors, shall, in the absence or disability of the President, perform the duties and exercise the powers of the President and shall perform such other duties and have such powers as the Board of Directors may, from time to time, determine or as these By-laws may prescribe.

4.8. Treasurer. The Treasurer shall have the care and custody of all the funds and securities of the Company that may come into his or her hands as Treasurer, and the power and authority to endorse checks, drafts and other instruments for the payment of money for deposit or collection when necessary or proper and to deposit the same to the credit of the Company in such bank or banks or depository as the Board of Directors, or the officers or agents to whom the Board of Directors may delegate such authority, may designate, and such officer may endorse all commercial documents requiring endorsements for or on behalf of the Company. The Treasurer may sign all receipts and vouchers for the payments made to the Company. The Treasurer shall render an account of such officer's transactions to the Board of Directors as often as the Board of Directors or the committee shall require the same. The Treasurer shall enter regularly in the books to be kept by such officer for that purpose full and adequate account of all moneys received and paid by him or her on account of the Company. The Treasurer shall perform all acts incident to the position of Treasurer, subject to the control of the Board of Directors. The Treasurer shall when requested, pursuant to vote of the Board of Directors, give a bond to the Company conditioned for the faithful performance of such officer's duties, the expense of which bond shall be borne by the Company.

4.9. Secretary. The Secretary shall keep the minutes of all meetings of the Board of Directors and of the stockholders; such officer shall attend to the giving and serving of all notices of the Company. Except as otherwise ordered by the Board of Directors, such officer shall attest the seal of the Company upon all contracts and instruments executed under such seal and shall affix the seal of the Company thereto and to all certificates of shares of capital stock of the Company. The Secretary shall have charge of the stock certificate book, transfer book and stock ledger, and such other books and papers as the Board of Directors may direct. The Secretary shall, in general, perform all the duties of Secretary, subject to the control of the Board of Directors.

4.10. Assistant Secretary. The Board of Directors or any two of the officers of the Company acting jointly may appoint or remove one or more Assistant Secretaries of the Company. Any Assistant Secretary upon such officer's appointment shall perform such duties of the Secretary, and also any and all such other duties as the Board of Directors or the President or a Vice-President or the Treasurer or the Secretary may designate.

4.11. Assistant Treasurer. The Board of Directors or any two of the officers of the Company acting jointly may appoint or remove one or more Assistant Treasurers of the Company. Any Assistant Treasurer upon such officer's appointment shall perform such of the duties of the Treasurer, and also any and all such other duties as the Board of Directors or the President or a Vice-President or the Treasurer or the Secretary may designate.

4.12. Subordinate Officers. The Board of Directors may select such subordinate officers as it may deem desirable. Each such officer shall hold office for such period, have such authority, and perform such duties as the Board of Directors may prescribe. The Board of Directors may, from time to time, authorize any officer to appoint and remove subordinate officers and to prescribe the powers and duties thereof.

4.13. Delegation of Authority. The Board of Directors may from time to time delegate the powers or duties of any officer to any other officer or agent, notwithstanding any provision hereof.

4.14. Removal. The Board of Directors may remove any officer of the Company at any time, with or without cause.

Article V. — Stock.

5.1. Stock. The shares of the Company's capital stock may be certificated or uncertificated and shall be entered in the books of the Company and registered as they are issued. Any certificate representing shares of stock issued to a stockholder of the Company (i) shall be numbered, (ii) shall certify the holder's name, the number of shares and the class or series of stock, (iii) shall otherwise be in such form as the Board of Directors shall prescribe, (iv) shall be signed by both of (a) either the President or a Vice-President, and (b) any one of the Treasurer or an Assistant Treasurer or the Secretary or an Assistant Secretary, and (v) shall be sealed with the corporate seal of the Company, if any. If such certificate is countersigned (l) by a transfer agent other than the Company or its employee, or, (2) by a registrar other than the Company or its employee, the signature of the officers of the Company and the corporate seal may be facsimiles. In case any officer or officers who shall have signed, or whose facsimile signature or signatures shall have been used on, any such

certificate or certificates shall cease to be such officer or officers of the Company, whether because of death, resignation or otherwise, before such certificate or certificates shall have been delivered by the Company, such certificate or certificates may nevertheless be adopted by the Company and be issued and delivered as though the person or persons who signed such certificate or certificates or whose facsimile signature shall have been used thereon had not ceased to be such officer or officers of the Company.

5.2. Fractional Share Interests. The Company may, but shall not be required to, issue fractions of a share. If the Company does not issue fractions of a share, it shall (i) arrange for the disposition of fractional interests by those entitled thereto, (ii) pay in cash the fair value of fractions of a share as of the time when those entitled to receive such fractions are determined, or (iii) issue scrip or warrants in registered or bearer form that shall entitle the holder to receive a certificate for a full share upon the surrender of such scrip or warrants aggregating a full share. A certificate for a fractional share shall, but scrip or warrants shall not unless otherwise provided therein, entitle the holder to exercise voting rights, to receive dividends thereon, and to participate in any of the assets of the Company in the event of liquidation. The Board of Directors may cause scrip or warrants to be issued subject to the conditions that they shall become void if not exchanged for certificates representing full shares before a specified date, or subject to the conditions that the shares for which scrip or warrants are exchangeable may be sold by the Company and the proceeds thereof distributed to the holders of scrip or warrants, or subject to any other conditions that the Board of Directors may impose.

5.3. Transfers of Stock.

Subject to any transfer restrictions then in force, the shares of stock of the Company shall be transferable only upon its books by the holders thereof in person or by their duly authorized attorneys or legal representatives.

If the shares of stock of the Company to be transferred are certificated shares, then, subject to the provisions of Section 5.7 below, the holder of the certificate or certificates representing such shares shall surrender to the Company or the transfer agent of the Company such certificate or certificates duly endorsed or accompanied by proper evidence of succession, assignation or authority to transfer, and, subject to any transfer restrictions then in force, the Company or the transfer agent of the Company shall cancel such certificate or certificates upon receipt thereof or upon compliance by such holder with the provisions of Section 5.7 below and (i) deliver to the applicable stockholder transferee either a new certificate or certificates representing the number of shares transferred or appropriate documentation evidencing the applicable stockholder transferee's record ownership of a number of uncertificated shares equal to the number of shares transferred, and, if applicable, (ii) deliver to the applicable stockholder transferor a new certificate or certificates representing the number of shares not transferred that were previously represented by the certificate or certificates so surrendered or appropriate documentation evidencing the applicable stockholder transferor's record ownership of a number of uncertificated shares equal to such number of shares not transferred. Any transfer or transfers in compliance with the provisions of this paragraph shall be recorded upon the books of the Company.

If the shares of stock of the Company to be transferred are uncertificated shares, then the registered owner of such shares shall deliver to the Company or the transfer agent of the Company proper transfer instructions, with such proof of authenticity of signature as the Company or its transfer agent or registrar may reasonably require, and, subject to any transfer restrictions then in force that are applicable to such shares, the Company or the transfer agent of the Company shall cancel such shares upon receipt of such transfer instructions and (i) deliver to the applicable stockholder transferee either a new certificate or certificates representing such shares or appropriate documentation evidencing the applicable stockholder transferee's record ownership of such shares in uncertificated form, and, if applicable and required, (ii) deliver to the applicable stockholder transferor appropriate documentation evidencing that the applicable stockholder transferor is no longer the record owner of such shares so transferred. Any transfer or transfers in compliance with the provisions of this paragraph shall be recorded upon the books of the Company.

The Company shall be entitled to treat the holder of record of any share or shares of stock as the holder in fact thereof and accordingly shall not be bound to recognize any equitable or other claim to or

interest in such share on the part of any other person whether or not it shall have express or other notice thereof save as expressly provided by the laws of Delaware.

5.4. Record Date. For the purpose of determining the stockholders entitled to notice of or to vote at any meeting of stockholders or any adjournment thereof, or entitled to receive payment of any dividend or other distribution or the allotment of any rights, or entitled to exercise any rights in respect of any change, conversion, or exchange of stock or for the purpose of any other lawful action, the Board of Directors may fix, in advance, a record date, that shall not be more than sixty (60) calendar days nor less than ten (10) calendar days before the date of such meeting, nor more than sixty (60) calendar days prior to any other action. If no such record date is fixed by the Board of Directors, the record date for determining stockholders entitled to notice of or to vote at a meeting of stockholders shall be at the close of business on the day before the day on which notice is given, or, if notice is waived, at the close of business on the day before the day on which the meeting is held; the record date for determining stockholders for any other purpose shall be at the close of business on the day on which the Board of Directors adopts the resolution relating thereto. A determination of stockholders of record entitled to notice of or to vote at any meeting of stockholders shall apply to any adjournment of the meeting; provided, however, that the Board of Directors may fix a new record date for the adjourned meeting.

5.5. Transfer Agent and Registrar. The Board of Directors may appoint one or more transfer agents or transfer clerks and one or more registrars and may require all certificates of stock to bear the signature or signatures of any of them.

5.6. Dividends.

(a) **Power to Declare.** Dividends upon the capital stock of the Company, subject to the provisions of the Company's Certificate of Incorporation, if any, may be declared by the Board of Directors at any regular or special meeting, pursuant to law. Dividends may be paid in cash, in property, or in shares of the capital stock, subject to the provisions of the Company's Certificate of Incorporation and the laws of Delaware.

(b) **Reserves.** Before payment of any dividend, there may be set aside out of any funds of the Company available for dividends such sum or sums as the directors from time to time, in their absolute discretion, think proper as a reserve or reserves to meet contingencies, or for equalizing dividends, or

for repairing or maintaining any property of the Company, or for such other purpose as the directors shall think conducive to the interest of the Company, and the directors may modify or abolish any such reserve in the manner in which it was created.

5.7. Lost, Stolen, or Destroyed Certificates. No certificates for shares of stock of the Company shall be issued in place of any certificate alleged to have been lost, stolen, or destroyed, except upon production of such evidence of the loss, theft, or destruction and upon indemnification of the Company and its agents to such extent and in such manner as the officers of the Company may from time to time prescribe. Upon compliance with the foregoing provisions of this Section 5.7, the Company may issue (i) a new certificate or certificates of stock or (ii) uncertificated shares, in place of any certificate or certificates previously issued by the Company alleged to have been lost, stolen or destroyed.

5.8. Inspection of Books. The stockholders of the Company, by a majority vote at any meeting of stockholders duly called, or in case the stockholders shall fail to act, the Board of Directors shall have power from time to time to determine whether and to what extent and at what times and places and under what conditions and regulations the accounts and books of the Company (other than the stock ledger) or any of them, shall be open to inspection of stockholders; and no stockholder shall have any

right to inspect any account or book or document of the Company except as conferred by statute or authorized by the Board of Directors or by a resolution of the stockholders.

Article VI. — Miscellaneous Management Provisions.

6.1. Checks, Drafts, and Notes. All checks, drafts, or orders for the payment of money, and all notes and acceptances of the Company shall be signed by such officer or officers, or such agent or agents, as the officers of the Company may designate.

6.2. Notices.

(a) Notices to directors may, and notices to stockholders shall, be in writing or by electronic transmission, and delivered personally, electronically transmitted or mailed to the directors or stockholders at their postage or electronic mail addresses appearing on the books of the Company. Notice by mail and electronic transmission shall be deemed to be given at the time when the same shall be mailed or transmitted. Notice to directors may also be given by telegram, facsimile or orally, by telephone or in person.

(b) Whenever any notice is required to be given under the provisions of any applicable statute or of the Company's Certificate of Incorporation or of these By-laws, an electronic transmission or written waiver of notice, signed by the person or persons entitled to said notice, whether before or after the time stated therein or the meeting or action to which such notice relates, shall be deemed equivalent to notice. Attendance of a person at a meeting shall constitute a waiver of notice of such meeting except when the person attends a meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened.

6.3. Conflict of Interest. No contract or transaction between the Company and one or more of its directors or officers, or between the Company and any other corporation, partnership, association, or other organization in which one or more of its directors or officers are directors or officers, or have a financial interest, shall be void or voidable solely for this reason, or solely because the director or officer is present at or participates in the meeting of the Board of Directors or committee thereof that authorized the contract or transaction, or solely because his, her, or their votes are counted for such purpose, if: (i) the material facts as to his, her or their relationship or interest and as to the contract or transaction are disclosed or are known to the Board of Directors or the committee and the Board of Directors or committee in good faith authorizes the contract or transaction by the affirmative vote of a majority of the disinterested directors, even though the disinterested directors may be less than a quorum; (ii) the material facts as to his, her or their relationship or interest and as to the contract or transaction are disclosed or are known to the stockholders of the Company entitled to vote thereon, and the contract or transaction as specifically approved in good faith by vote of such stockholders; or (iii) the contract or transaction is fair as to the Company as of the time it is authorized, approved, or ratified, by the Board of Directors, a committee or the stockholders. Common or interested directors may be counted in determining the presence of a quorum at a meeting of the Board of Directors or of a committee that authorizes the contract or transaction.

6.4. Voting of Securities owned by the Company. Subject always to the specific directions of the Board of Directors, (i) any shares or other securities issued by any other corporation and owned or controlled by the Company may be voted in person at any meeting of security holders of such other corporation by the President of the Company if he or she is present at such meeting, or in his or her absence by the Treasurer of the Company if he or she is present at such meeting, and (ii) whenever, in the judgment of the President, it is desirable for the Company to execute a proxy or written consent in respect to any shares or other securities issued by any other corporation and owned by the Company, such proxy

or consent shall be executed in the name of the Company by the President, without the necessity of any authorization by the Board of Directors, affixation of corporate seal or countersignature or attestation by another officer, provided that if the President is unable to execute such proxy or consent by reason of sickness, absence from the United States or other similar cause, the Treasurer may execute such proxy or consent. Any person or persons designated in the manner above stated as the proxy or proxies of the Company shall have full right, power and authority to vote the shares or other securities issued by such other corporation and owned by the Company the same as such shares or other securities might be voted by the Company.

Article VII. — Indemnification.

7.1. Right to Indemnification. Each person who was or is made a party or is threatened to be made a party to or is otherwise involved in any action, suit or proceeding, whether civil, criminal, administrative or investigative (a "Proceeding"), by reason of being or having been a director or officer of the Company or serving or having served at the request of the Company as a director, trustee, officer, employee or agent of another corporation or of a partnership, joint venture, trust or other enterprise, including service with respect to an employee benefit plan (an "Indemnitee"), whether the basis of such proceeding is alleged action or failure to act in an official capacity as a director, trustee, officer, employee or agent or in any other capacity while serving as a director, trustee, officer, employee or agent, shall be indemnified and held harmless by the Company to the fullest extent authorized by the DGCL, as the same exists or may hereafter be amended (but, in the case of any such amendment, only to the extent that such amendment permits the Company to provide

broader indemnification rights than permitted prior thereto) (as used in this Article 7, the “Delaware Law”), against all expense, liability and loss (including attorneys’ fees, judgments, fines, ERISA excise taxes or penalties and amounts paid in settlement) reasonably incurred or suffered by such Indemnitee in connection therewith and such indemnification shall continue as to an Indemnitee who has ceased to be a director, trustee, officer, employee, or agent and shall inure to the benefit of the Indemnitee’s heirs, executors, and administrators; provided, however, that, except as provided in Section 7.2 hereof with respect to Proceedings to enforce rights to indemnification, the Company shall indemnify any such Indemnitee in connection with a Proceeding (or part thereof) initiated by such Indemnitee only if such Proceeding (or part thereof) was authorized by the Board of Directors of the Company. The right to indemnification conferred in this Article 7 shall be a contract right and shall include the right to be paid by the Company the expenses (including attorneys’ fees) incurred in defending any such Proceeding in advance of its final disposition (an “Advancement of Expenses”); provided, however, that, if the Delaware Law so requires, an Advancement of Expenses incurred by an Indemnitee shall be made only upon delivery to the Company of an undertaking (an “Undertaking”), by or on behalf of such Indemnitee, to repay all amounts so advanced if it shall ultimately be determined by final judicial decision from which there is no further right to appeal (a “Final Adjudication”) that such Indemnitee is not entitled to be indemnified for such expenses under this Article 7 or otherwise.

7.2. Right of Indemnitee to Bring Suit. If a claim under Section 7.1 hereof is not paid in full by the Company within sixty (60) days after a written claim has been received by the Company, except in the case of a claim for an Advancement of Expenses, in which case the applicable period shall be twenty (20) days, the Indemnitee may at any time thereafter bring suit against the Company to recover the unpaid amount of the claim. If successful in whole or in part in any such suit, or in a suit brought by the Company to recover an Advancement of Expenses pursuant to the terms of an Undertaking, the Indemnitee shall be entitled to be paid also the expense of prosecuting or defending such suit. In any suit brought by the Indemnitee to enforce a right to indemnification hereunder (but not in a suit brought by the Indemnitee to enforce a right to an Advancement of Expenses) it shall be a defense that the Indemnitee has not met the applicable standard of conduct set forth in the Delaware Law. In addition, any suit by the Company to recover an Advancement of Expenses pursuant to the terms of an Undertaking the Company

shall be entitled to recover such expenses upon a Final Adjudication that, the Indemnitee has not met the applicable standard of conduct set forth in the Delaware Law. Neither the failure of the Company (including its Board of Directors, independent legal counsel, or its stockholders) to have made a determination prior to the commencement of such suit that indemnification of the Indemnitee is proper in the circumstances because the Indemnitee has met the applicable standard of conduct set forth in the Delaware Law, nor an actual determination by the Company (including its Board of Directors, independent legal counsel, or its stockholders) that the Indemnitee has not met such applicable standard of conduct, shall create a presumption that the Indemnitee has not met the applicable standard of conduct or, in the case of such a suit brought by the Indemnitee, be a defense to such suit. In any suit brought by the Indemnitee to enforce a right to indemnification or to an Advancement of Expenses hereunder, or by the Company to recover an Advancement of Expenses pursuant to the terms of an Undertaking, the burden of proving that the Indemnitee is not entitled to be indemnified, or to such Advancement of Expenses, under this Article 7 or otherwise shall be on the Company.

7.3. Non-Exclusivity of Rights. The rights to indemnification and to the Advancement of Expenses conferred in this Article 7 shall not be exclusive of any other right that any person may have or hereafter acquire under any statute, the Company’s Certificate of Incorporation, by law, agreement, vote of stockholders or disinterested directors or otherwise.

7.4. Insurance. The Company may maintain insurance, at its expense, to protect itself and any director, officer, employee or agent of the Company or another corporation, partnership, joint venture, trust or other enterprise against any expense, liability or loss, whether or not the Company would have the power to indemnify such person against such expense, liability or loss under this Article 7 or under the Delaware Law.

7.5. Indemnification of Employees and Agents of the Company. The Company may, to the extent authorized from time to time by the Board of Directors, grant rights to indemnification, and to the Advancement of Expenses, to any employee or agent of the Company to the fullest extent of the provisions of this Article 7 with respect to the indemnification and Advancement of Expenses of directors and officers of the Company.

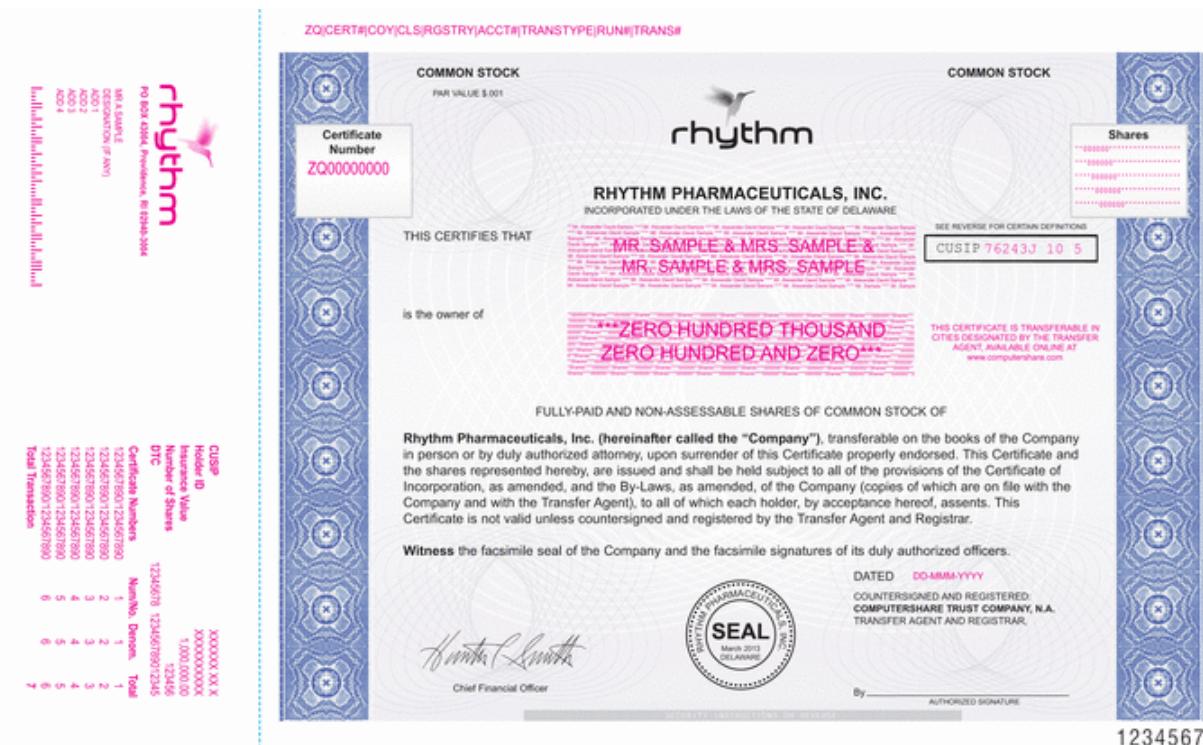
7.6. Merger or Consolidation. For purposes of this Article 7, references to the “Company” shall include, in addition to the resulting corporation, any constituent corporation (including any constituent of a constituent) absorbed in a consolidation or merger which, if its separate existence had continued, would have had power and authority to indemnify its directors, officers and employees or agents, so that any person who is or was a director, officer, employee or agent of such constituent corporation, or is or was serving at the request of such constituent corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, shall stand in the same position under this Article 7 with respect to the resulting or surviving corporation as he or she would have with respect to such constituent corporation if its separate existence had continued

7.7. Savings Clause. If this Article 7 or any portion hereof shall be invalidated on any ground by any court of competent jurisdiction, then the Company shall nevertheless indemnify and advance expenses to each person entitled to indemnification under Article 7 as to all expense, liability and loss (including attorneys’ fees and related disbursements, judgments, fines, ERISA excise taxes and penalties, penalties and amounts paid or to be paid in settlement) actually and reasonably incurred or suffered by such person and for which indemnification or advancement of expenses is available to such person pursuant to this Article 7 to the fullest extent permitted by any applicable portion of this Article 7 that shall not have been invalidated and to the fullest extent permitted by applicable law.

Article VIII. — Amendments.

8.1. Amendments. Subject always to any limitations imposed by the Company’s Certificate of Incorporation, these By-laws and any amendment thereof may be altered, amended or repealed, or new by-laws may be adopted, by the Board of Directors at any regular or special meeting by the affirmative vote of a majority of all of the members of the Board of Directors, provided in the case of any special meeting at which all of the members of the Board of Directors are not present, that the notice of such meeting shall have stated that the amendment of these By-laws was one of the purposes of the meeting; but these By-laws and any amendment thereof, including the By-laws adopted by the Board of Directors, may be altered, amended or repealed and other By-laws may be adopted by the affirmative vote of holders of at least seventy-five percent (75%) of the outstanding shares of capital stock of the Company entitled to vote in the election of directors or class of directors, voting together as a single class, provided, in the case of any special meeting, that notice of such proposed alteration, amendment, repeal or adoption is included in the notice of the meeting.

* * *



RHYTHM PHARMACEUTICALS, INC.

THE COMPANY WILL FURNISH WITHOUT CHARGE TO EACH SHAREHOLDER WHO SO REQUESTS, A SUMMARY OF THE POWERS, DESIGNATIONS, PREFERENCES AND RELATIVE, PARTICIPATING, OPTIONAL OR OTHER SPECIAL RIGHTS OF EACH CLASS OF STOCK OF THE COMPANY AND THE QUALIFICATIONS, LIMITATIONS OR RESTRICTIONS OF SUCH PREFERENCES AND RIGHTS, AND THE VARIATIONS IN RIGHTS, PREFERENCES AND LIMITATIONS DETERMINED FOR EACH SERIES, WHICH ARE FIXED BY THE CERTIFICATE OF INCORPORATION OF THE COMPANY, AS AMENDED, AND THE RESOLUTIONS OF THE BOARD OF DIRECTORS OF THE COMPANY, AND THE AUTHORITY OF THE BOARD OF DIRECTORS TO DETERMINE VARIATIONS FOR FUTURE SERIES. SUCH REQUEST MAY BE MADE TO THE OFFICE OF THE SECRETARY OF THE COMPANY OR TO THE TRANSFER AGENT. THE BOARD OF DIRECTORS MAY REQUIRE THE OWNER OF A LOST OR DESTROYED STOCK CERTIFICATE, OR HIS LEGAL REPRESENTATIVES, TO GIVE THE COMPANY A BOND TO INDEMNIFY IT AND ITS TRANSFER AGENTS AND REGISTRARS AGAINST ANY CLAIM THAT MAY BE MADE AGAINST THEM ON ACCOUNT OF THE ALLEGED LOSS OR DESTRUCTION OF ANY SUCH CERTIFICATE.

The following abbreviations, when used in the inscription on the face of this certificate, shall be construed as though they were written out in full according to applicable laws or regulations:

TEN COM - as tenants in common	UNIF GIFT MIN ACT - under Uniform Gifts to Minors Act.....	Custodian (Name) _____ (State) _____
TEN ENT - as tenants by the entireties	UNIF TRF MIN ACT - under Uniform Transfers to Minors Act	Custodian (until age (Name) _____ (State) _____
JT TEN - as joint tenants with right of survivorship and not as tenants in common

Additional abbreviations may also be used though not in the above list.

PLEASE INSERT SOCIAL SECURITY OR OTHER IDENTIFYING NUMBER OF ASSIGNEE

For value received, _____ hereby sell, assign and transfer unto _____

(PLEASE PRINT OR TYPE WRITING NAME AND ADDRESS, INCLUDING POSTAL ZIP CODE, OF ASSIGNEE)

of the capital stock represented by the within Certificate, and do hereby irrevocably constitute and appoint _____ Shares
to transfer the said stock on the books of the within-named Company with full power of substitution in the premises.

Dated: _____ 20_____

Signature: _____

Signature: _____

Notice: The signature to this assignment must correspond with the name
as written upon the face of the certificate, in every particular,
without alteration or enlargement, or any change whatever.

Signature(s) Guaranteed: Medallion Guarantee Stamp
THE SIGNATURE(S) SHOULD BE GUARANTEED BY AN ELIGIBLE GUARANTOR INSTITUTION (Banks,
Stockbrokers, Savings and Loan Associations and Credit Unions) WITH MEMBERSHIP IN AN APPROVED
SIGNATURE GUARANTEE MEDALLION PROGRAM, PURSUANT TO S.E.C. RULE 17Ad-15.

SECURITY INSTRUCTIONS

THIS IS WATERMARKED PAPER. DO NOT ACCEPT WITHOUT NOTING
WATERMARK. HOLD TO LIGHT TO VERIFY WATERMARK.



The IRS requires that we report the cost basis of certain shares acquired after January 1, 2011. If your shares were covered by the legislation and you have sold or transferred the shares and requested a specific cost basis calculation method, we have processed as requested. If you did not specify a cost basis calculation method, we have defaulted to the first in, first out (FIFO) method. Please visit our website or consult your tax advisor if you need additional information about cost basis.

If you do not keep in contact with us or do not have any activity in your account for the time periods specified by state law, your property could become subject to state unclaimed property laws and transferred to the appropriate state.

134261

September 25, 2017

Rhythm Pharmaceuticals, Inc.
500 Boylston Street, 11th Floor
Boston, MA 02116

Re: Form S-1 Registration Statement File No. 333-220337 Initial Public Offering of up to \$115,000,000 of shares of Common Stock of Rhythm Pharmaceuticals, Inc.

Ladies and Gentlemen:

We have acted as counsel to Rhythm Pharmaceuticals, Inc., a Delaware corporation (the "Company"), in connection with the registration by the Company of up to \$115,000,000 of shares of common stock of the Company, par value \$0.001 per share (the "Shares").

The Shares are included in a registration statement on Form S-1 under the Securities Act of 1933, as amended (the "Act"), filed with the Securities and Exchange Commission (the "Commission") on September 25, 2017 (Registration No. 333-220337) (the "Registration Statement"). This opinion is being furnished in connection with the requirements of Item 601(b)(5) of Regulation S-K under the Act, and no opinion is expressed herein as to any matter pertaining to the contents of the Registration Statement or the related prospectus (the "Prospectus"), other than as expressly stated herein with respect to the issuance of the Shares.

As such counsel, we have examined such matters of fact and questions of law as we have considered appropriate for purposes of this letter. With your consent, we have relied upon certificates and other assurances of officers of the Company and others as to factual matters without having independently verified such factual matters. We are opining herein as to the General Corporation Law of the State of Delaware (the "DGCL"), and we express no opinion with respect to any other laws.

Subject to the foregoing and the other matters set forth herein, it is our opinion that, as of the date hereof, when the Shares shall have been duly registered on the books of the transfer agent and registrar therefor in the name or on behalf of the purchasers and have been issued by the Company against payment therefor in the circumstances contemplated by the form of underwriting agreement most recently filed as an exhibit to the Registration Statement, the issue and sale of the Shares will have been duly authorized by all necessary corporate action of the Company, and the Shares will be validly issued, fully paid, and nonassessable. In rendering the foregoing opinion, we have assumed that the Company will comply with all applicable notice requirements regarding uncertificated shares provided in the DGCL.

This opinion is for your benefit in connection with the Registration Statement and may be relied upon by you and by persons entitled to rely upon it pursuant to the applicable provisions of the Act. We consent to your filing this opinion as an exhibit to the Registration Statement and to the reference to our firm in the

Prospectus under the heading "Legal Matters". In giving such consent, we do not thereby admit that we are in the category of persons whose consent is required under Section 7 of the Act or the rules and regulations of the Commission thereunder.

Very truly yours,

/s/ MORGAN, LEWIS & BOCKIUS LLP

INDEMNIFICATION AGREEMENT

This Indemnification Agreement ("Agreement"), dated as of [], 2017, is by and between Rhythm Pharmaceuticals, Inc., a Delaware corporation (the "Company") and [NAME OF DIRECTOR/OFFICER](1) ("Indemnitee").

WHEREAS, Indemnitee is [a director/an officer] of the Company;

WHEREAS, both the Company and Indemnitee recognize the increased risk of litigation and other claims being asserted against directors and officers of public companies;

WHEREAS, the board of directors of the Company (the "Board") has determined that enhancing the ability of the Company to retain and attract as directors and officers the most capable persons is in the best interests of the Company and that the Company therefore should seek to assure such persons that indemnification and insurance coverage is available; and

WHEREAS, in recognition of the need to provide Indemnitee with substantial protection against personal liability, in order to procure Indemnitee's [continued] service as a [director/officer] of the Company and to enhance Indemnitee's ability to serve the Company in an effective manner, and in order to provide such protection pursuant to express contract rights (intended to be enforceable irrespective of, among other things, any amendment to the Company's certificate of incorporation or bylaws (collectively, the "Constituent Documents"), any change in the composition of the Board or any change in control or business combination transaction relating to the Company), the Company wishes to provide in this Agreement for the indemnification of, and the advancement of Expenses (as defined in Section 1(f) below) to, Indemnitee as set forth in this Agreement and for the [continued] coverage of Indemnitee under the Company's directors' and officers' liability insurance policies.

NOW, THEREFORE, in consideration of the foregoing and Indemnitee's agreement to continue to provide services to the Company, the parties agree as follows:

1. Definitions. For purposes of this Agreement, the following terms shall have the following meanings:

(a) "Beneficial Owner" has the meaning given to the term "beneficial owner" in Rule 13d-3 under the Securities Exchange Act of 1934, as amended (the "Exchange Act").

(b) "Change in Control" means the occurrence after the date of this Agreement of any of the following events:

(i) any Person is or becomes the Beneficial Owner, directly or indirectly, of securities of the Company representing 50% or more of the Company's then outstanding Voting Securities unless the change in relative Beneficial Ownership of the Company's securities by any Person results solely from a reduction in the aggregate number of outstanding shares of securities entitled to vote generally in the election of directors;

(1) Bracketed language throughout document to be customized as appropriate.

(ii) the consummation of a reorganization, merger or consolidation, unless immediately following such reorganization, merger or consolidation, all of the Beneficial Owners of the Voting Securities of the Company immediately prior to such transaction beneficially own, directly or indirectly, more than 50% of the combined voting power of the outstanding Voting Securities of the entity resulting from such transaction;

(iii) during any period of two consecutive years, not including any period prior to the execution of this Agreement, individuals who at the beginning of such period constituted the Board (including for this purpose any new directors whose election by the Board or nomination for election by the Company's stockholders was approved by a vote of at least two-thirds (2/3) of the directors then still in office who either were directors at the beginning of the period or whose election or nomination for election was previously so approved) cease for any reason to constitute at least a majority of the Board; or

(iv) the stockholders of the Company approve a plan of complete liquidation or dissolution of the Company or an agreement for the sale or disposition by the Company of all or substantially all of the Company's assets.

(c) "Claim" means:

(i) any threatened, pending or completed action, suit, proceeding or alternative dispute resolution mechanism, whether civil, criminal, administrative, arbitrative, investigative or other, and whether made pursuant to federal, state or other law; or

(ii) any inquiry, hearing or investigation that Indemnitee determines might lead to the institution of any such action, suit, proceeding or alternative dispute resolution mechanism.

(d) "Delaware Court" shall have the meaning ascribed to it in Section 8(e) below.

(e) "Disinterested Director" means a director of the Company who is not and was not a party to the Claim in respect of which indemnification is sought by Indemnitee.

(f) "Expenses" means any and all expenses, including attorneys' and experts' fees, reasonably incurred, court costs, transcript costs, travel expenses, duplicating, printing and binding costs, telephone charges, and all other costs and expenses incurred in connection with investigating, defending, being a witness in or participating in (including on appeal), or preparing to defend, be a witness or participate in, any Claim. Expenses also shall include (i) Expenses incurred in connection with any appeal resulting from any Claim, including without limitation the premium, security for, and other costs relating to any cost bond, supersedeas bond, or other appeal bond or its equivalent, and (ii) for purposes of Section 4 only, Expenses incurred by Indemnitee in connection with the interpretation, enforcement or defense of Indemnitee's rights under this Agreement, by litigation or otherwise. Expenses, however, shall

not include amounts paid in settlement by Indemnitee or the amount of judgments or fines against Indemnitee. The parties agree that for the purposes of any advancement of Expenses for which Indemnitee has made written demand to the Company in accordance with this Agreement, all Expenses included in such demand that are certified by

affidavit of Indemnitee's counsel as being reasonable shall be presumed conclusively to be reasonable.

(g) "Expense Advance" means any payment of Expenses advanced to Indemnitee by the Company pursuant to Section 3 or Section 4 hereof.

(h) "Indemnifiable Event" means any event or occurrence, whether occurring before, on or after the date of this Agreement, related to the fact that Indemnitee is or was a director, officer, employee or agent of the Company or any subsidiary of the Company, or is or was serving at the request of the Company as a director, officer, employee, member, manager, trustee or agent of any other corporation, limited liability company, partnership, joint venture, trust or other entity or enterprise (collectively with the Company, "Enterprise") or by reason of an action or inaction by Indemnitee in any such capacity (whether or not serving in such capacity at the time any Loss is incurred for which indemnification can be provided under this Agreement).

(i) "Independent Counsel" means a law firm, or a member of a law firm, that is experienced in matters of corporation law and neither presently performs, nor in the past five (5) years has performed, services for either: (i) the Company or Indemnitee (other than in connection with matters concerning Indemnitee under this Agreement or of other indemnitees under similar agreements) or (ii) any other party to the Claim giving rise to a claim for indemnification hereunder. Notwithstanding the foregoing, the term "Independent Counsel" shall not include any person who, under the applicable standards of professional conduct then prevailing, would have a conflict of interest in representing either the Company or Indemnitee in an action to determine Indemnitee's rights under this Agreement.

(j) "Losses" means any and all Expenses, damages, losses, liabilities, judgments, fines, penalties (whether civil, criminal or other), ERISA excise taxes, amounts paid or payable in settlement, including any interest, assessments, any federal, state, local or foreign taxes imposed as a result of the actual or deemed receipt of any payments under this Agreement and all other charges paid or payable in connection with investigating, defending, being a witness in or participating in (including on appeal), or preparing to defend, be a witness or participate in, any Claim.

(k) "Person" means any individual, corporation, firm, partnership, joint venture, limited liability company, estate, trust, business association, organization, governmental entity or other entity and includes the meaning set forth in Sections 13(d) and 14(d) of the Exchange Act.

(l) "Standard of Conduct Determination" shall have the meaning ascribed to it in Section 8(b) below.

(m) "Voting Securities" means any securities of the Company that vote generally in the election of directors.

2. Indemnification. Subject to Section 8 and Section 9 of this Agreement, the Company shall indemnify Indemnitee, to the fullest extent permitted by the laws of the State of Delaware in effect on the date hereof, or as such laws may from time to time hereafter be amended to

increase the scope of such permitted indemnification, against any and all Losses if Indemnitee was or is or becomes a party to or participant in, or is threatened to be made a party to or participant in, any Claim by reason of or arising in part out of an Indemnifiable Event, including, without limitation, Claims brought by or in the right of the Company, Claims brought by third parties, and Claims in which Indemnitee is solely a witness.

3. Advancement of Expenses. Indemnitee shall have the right to advancement by the Company, prior to the final disposition of any Claim by final adjudication to which there are no further rights of appeal, of any and all Expenses actually and reasonably paid or incurred by Indemnitee in connection with any Claim arising out of an Indemnifiable Event. Indemnitee's right to such advancement is not subject to the satisfaction of any standard of conduct. Without limiting the generality or effect of the foregoing, within thirty (30) days after any request by Indemnitee, the Company shall, in accordance with such request, (a) pay such reasonable Expenses on behalf of Indemnitee, (b) advance to Indemnitee funds in an amount sufficient to pay such Expenses, or (c) reimburse Indemnitee for such Expenses. In connection with any request for Expense Advances, Indemnitee shall not be required to provide any documentation or information to the extent that the provision thereof would undermine or otherwise jeopardize attorney-client privilege. In connection with any request for Expense Advances, Indemnitee shall execute and deliver to the Company an undertaking (which shall be accepted without reference to Indemnitee's ability to repay the Expense Advances) to repay any amounts paid, advanced, or reimbursed by the Company for such Expenses to the extent that it is ultimately determined, following the final disposition of such Claim by final adjudication to which there are no further rights of appeal, that Indemnitee is not entitled to indemnification hereunder. Indemnitee's obligation to reimburse the Company for Expense Advances shall be unsecured and no interest shall be charged thereon.

4. Indemnification for Expenses in Enforcing Rights. To the fullest extent allowable under applicable law, the Company shall also indemnify against, and, if requested by Indemnitee, shall advance to Indemnitee subject to and in accordance with Section 3, any Expenses actually and reasonably paid or incurred by Indemnitee in connection with any action or proceeding by Indemnitee for (a) indemnification or reimbursement or advance payment of Expenses by the Company under any provision of this Agreement, or under any other agreement or provision of the Constituent Documents now or hereafter in effect relating to Claims relating to Indemnifiable Events, and/or (b) recovery under any directors' and officers' liability insurance policies maintained by the Company, regardless of whether Indemnitee ultimately is determined to be entitled to such indemnification or insurance recovery, as the case may be. However, in the event that Indemnitee is ultimately determined not to be entitled to such indemnification or insurance recovery, as the case may be, then all amounts advanced under this Section 4 shall be repaid. Indemnitee shall be required to reimburse the Company in the event that a final judicial determination by final adjudication to which there are no further rights of appeal is made that such action brought by Indemnitee was frivolous or not made in good faith.

5. Partial Indemnity. If Indemnitee is entitled under any provision of this Agreement to indemnification by the Company for a portion of any Losses in respect of a Claim related to an Indemnifiable Event but not for the total amount thereof, the Company shall nevertheless indemnify Indemnitee for the portion thereof to which Indemnitee is entitled.

6. Notification and Defense of Claims.

(a) Notification of Claims. Indemnitee shall notify the Company in writing as soon as practicable of any Claim which could relate to an Indemnifiable Event or for which Indemnitee could seek Expense Advances, including a brief description (based upon information then available to Indemnitee) of the alleged facts underlying, such Claim. The failure by Indemnitee to timely notify the Company hereunder shall not relieve the Company from any liability hereunder unless the Company's ability to participate in the defense of such claim was materially and adversely affected by such failure/except that the Company shall not be liable to indemnify Indemnitee under this Agreement with respect to any judicial award in a Claim related to an Indemnifiable Event if the Company was not given a reasonable and timely opportunity to participate at its expense in the defense of such action. If at the time of the receipt of such notice, the Company has directors' and officers' liability insurance in effect under which coverage for Claims related to Indemnifiable Events is potentially available, the Company shall give prompt written notice to the applicable insurers in accordance with the procedures set forth in the applicable policies. The Company shall provide to Indemnitee a copy of such notice delivered to the applicable insurers, and copies of all subsequent correspondence between the Company and such insurers regarding the Claim, in each case substantially concurrently with the delivery or receipt thereof by the Company.

(b) Defense of Claims. The Company shall be entitled to participate in the defense of any Claim relating to an Indemnifiable Event at its own expense and, except as otherwise provided below, to the extent the Company so wishes, it may assume the defense thereof with counsel reasonably satisfactory to Indemnitee. After notice from the Company to Indemnitee of its election to assume the defense of any such Claim, the Company shall not be liable to Indemnitee under this Agreement or otherwise for any Expenses subsequently directly incurred by Indemnitee in connection with Indemnitee's defense of such Claim other than reasonable costs of investigation or as otherwise provided below. Indemnitee shall have the right to employ its own legal counsel in such Claim, but all Expenses related to such counsel incurred after notice from the Company of its assumption of the defense shall be at Indemnitee's own expense; provided, however, that if (i) Indemnitee's employment of its own legal counsel has been authorized by the Company, (ii) Indemnitee has reasonably determined that there may be a conflict of interest between Indemnitee and the Company in the defense of such Claim, (iii) after a Change in Control, Indemnitee's employment of its own counsel has been approved by the Independent Counsel or (iv) the Company shall not in fact have employed counsel to assume the defense of such Claim, then Indemnitee shall be entitled to retain its own separate counsel (but not more than one law firm plus, if applicable, local counsel in respect of any such Claim) and all Expenses related to such separate counsel shall be borne by the Company.

7. Procedure upon Application for Indemnification. In order to obtain indemnification pursuant to this Agreement, Indemnitee shall submit to the Company a written request therefor, including in such request such documentation and information as is reasonably available to Indemnitee and is reasonably necessary to determine whether and to what extent Indemnitee is entitled to indemnification following the final disposition of the Claim by final adjudication to which there are no further rights of appeal, provided that documentation and information need not be so provided to the extent that the provision thereof would undermine or otherwise

jeopardize attorney-client privilege. Indemnification shall be made insofar as the Company determines Indemnitee is entitled to indemnification in accordance with Section 8 below.

8. Determination of Right to Indemnification.

(a) Mandatory Indemnification; Indemnification as a Witness.

(i) To the extent that Indemnitee shall have been successful on the merits or otherwise in defense of any Claim relating to an Indemnifiable Event or any portion thereof or in defense of any issue or matter therein, including without limitation dismissal without prejudice, Indemnitee shall be indemnified against all Losses relating to such Claim in accordance with Section 2 to the fullest extent allowable by law, and no Standard of Conduct Determination (as defined in Section 8(b)) shall be required.

(ii) To the extent that Indemnitee's involvement in a Claim relating to an Indemnifiable Event is to prepare to serve and serve as a witness, and not as a party, Indemnitee shall be indemnified against all Losses incurred in connection therewith to the fullest extent allowable by law and no Standard of Conduct Determination (as defined in Section 8(b)) shall be required.

(b) Standard of Conduct. To the extent that the provisions of Section 8(a) are inapplicable to a Claim related to an Indemnifiable Event that shall have been finally disposed of, any determination of whether Indemnitee has satisfied any applicable standard of conduct under Delaware law that is a legally required condition to indemnification of Indemnitee hereunder against Losses relating to such Claim and any determination that Expense Advances must be repaid to the Company (a "Standard of Conduct Determination") shall be made as follows:

(i) if no Change in Control has occurred, (A) by a majority vote of the Disinterested Directors, even if less than a quorum of the Board, (B) by a committee of Disinterested Directors designated by a majority vote of the Disinterested Directors, even though less than a quorum or (C) if there are no such Disinterested Directors, by Independent Counsel in a written opinion addressed to the Board, a copy of which shall be delivered to Indemnitee; and

(ii) if a Change in Control shall have occurred, (A) if Indemnitee so requests in writing, by a majority vote of the Disinterested Directors, even if less than a quorum of the Board or (B) otherwise, by Independent Counsel in a written opinion addressed to the Board, a copy of which shall be delivered to Indemnitee.

The Company shall indemnify and hold harmless Indemnitee against and, if requested by Indemnitee, shall reimburse Indemnitee for, or advance to Indemnitee, within thirty (30) days of such request, any and all Expenses incurred by Indemnitee in cooperating with the person or persons making such Standard of Conduct Determination.

(c) Making the Standard of Conduct Determination. The Company shall use its reasonable best efforts to cause any Standard of Conduct Determination required under Section

8(b) to be made as promptly as practicable. If the person or persons designated to make the Standard of Conduct Determination under Section 8(b) shall not have made a determination within sixty (60) days after the later of (A) receipt by the Company of a written request from Indemnitee for indemnification pursuant to Section 7 (the date of such receipt being the “Notification Date”) and (B) the selection of an Independent Counsel, if such determination is to be made by Independent Counsel, then Indemnitee shall be deemed to have satisfied the applicable standard of conduct; provided that such sixty (60)-day period may be extended for a reasonable time, not to exceed an additional sixty (60) days if the person or persons making such determination in good faith requires such additional time to obtain or evaluate information relating thereto. Notwithstanding anything in this Agreement to the contrary, no determination as to entitlement of Indemnitee to indemnification under this Agreement shall be required to be made prior to the final disposition of any Claim by final adjudication to which there are no further rights of appeal.

(d) Payment of Indemnification. If, in regard to any Losses:

- (i) Indemnitee shall be entitled to indemnification pursuant to Section 8(a); and either
- (ii) no Standard Conduct Determination is legally required as a condition to indemnification of Indemnitee hereunder; or
- (iii) Indemnitee has been determined or deemed pursuant to Section 8(b) or Section 8(c) to have satisfied the Standard of Conduct

Determination,

then the Company shall pay to Indemnitee, within fifteen (15) days after the later of (A) the Notification Date or (B) the earliest date on which the applicable criterion specified in clause (i), (ii) or (iii) is satisfied, an amount equal to such Losses.

(e) Selection of Independent Counsel for Standard of Conduct Determination. If a Standard of Conduct Determination is to be made by Independent Counsel pursuant to Section 8(b)(i), the Independent Counsel shall be selected by the Board of Directors, and the Company shall give written notice to Indemnitee advising [him/her] of the identity of the Independent Counsel so selected. If a Standard of Conduct Determination is to be made by Independent Counsel pursuant to Section 8(b)(ii), the Independent Counsel shall be selected by Indemnitee, and Indemnitee shall give written notice to the Company advising it of the identity of the Independent Counsel so selected. In either case, Indemnitee or the Company, as applicable, may, within ten (10) days after receiving written notice of selection from the other, deliver to the other a written objection to such selection; provided, however, that such objection may be asserted only on the ground that the Independent Counsel so selected does not satisfy the criteria set forth in the definition of “Independent Counsel” in Section 1(i), and the objection shall set forth with particularity the factual basis of such assertion. Absent a proper and timely objection, the person or firm so selected shall act as Independent Counsel. If such written objection is properly and timely made and substantiated, (i) the Independent Counsel so selected may not serve as Independent Counsel unless and until such objection is withdrawn or a court has determined that such objection is without merit; and (ii) the non-objecting party may, at its option, select an

alternative Independent Counsel and give written notice to the other party advising such other party of the identity of the alternative Independent Counsel so selected, in which case the provisions of the two immediately preceding sentences, the introductory clause of this sentence and numbered clause (i) of this sentence shall apply to such subsequent selection and notice. If applicable, the provisions of clause (ii) of the immediately preceding sentence shall apply to successive alternative selections. If no Independent Counsel that is permitted under the foregoing provisions of this Section 8(e) to make the Standard of Conduct Determination shall have been selected within thirty (30) days after the Company gives its initial notice pursuant to the first sentence of this Section 8(e) or Indemnitee gives its initial notice pursuant to the second sentence of this Section 8(e), as the case may be, either the Company or Indemnitee may petition the Court of Chancery of the State of Delaware (“Delaware Court”) to resolve any objection which shall have been made by the Company or Indemnitee to the other’s selection of Independent Counsel and/or to appoint as Independent Counsel a person to be selected by the Court or such other person as the Court shall designate, and the person or firm with respect to whom all objections are so resolved or the person or firm so appointed will act as Independent Counsel. In all events, the Company shall pay all of the reasonable fees and expenses of the Independent Counsel incurred in connection with the Independent Counsel’s determination pursuant to Section 8(b).

(f) Presumptions and Defenses.

(i) Indemnitee’s Entitlement to Indemnification. In making any Standard of Conduct Determination, the person or persons making such determination shall presume that Indemnitee has satisfied the applicable standard of conduct and is entitled to indemnification, and the Company shall have the burden of proof to overcome that presumption and establish that Indemnitee is not so entitled. Any Standard of Conduct Determination that is adverse to Indemnitee may be challenged by Indemnitee in the Delaware Court. No determination by the Company (including by its directors or any Independent Counsel) that Indemnitee has not satisfied any applicable standard of conduct may be used as a defense to any legal proceedings brought by Indemnitee to secure indemnification or reimbursement or advance payment of Expenses by the Company hereunder or create a presumption that Indemnitee has not met any applicable standard of conduct.

(ii) Reliance as a Safe Harbor. For purposes of this Agreement, and without creating any presumption as to a lack of good faith if the following circumstances do not exist, Indemnitee shall be deemed to have acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the Company if Indemnitee’s actions or omissions to act are taken in good faith reliance upon the records of the Company, including its financial statements, or upon information, opinions, reports or statements furnished to Indemnitee by the officers or employees of the Company or any of its subsidiaries in the course of their duties, or by committees of the Board or by any other Person (including legal counsel, accountants and financial advisors) as to matters Indemnitee reasonably believes are within such other Person’s professional or expert competence and who has been selected with reasonable care by or on behalf of the Company. In addition, the knowledge and/or actions, or failures to act, of any director, officer, agent or employee of the Company shall not be imputed to Indemnitee for purposes of determining the right to indemnity hereunder.

(iii) **No Other Presumptions.** For purposes of this Agreement, the termination of any Claim by judgment, order, settlement (whether with or without court approval) or conviction, or upon a plea of nolo contendere or its equivalent, will not create a presumption that Indemnitee did not meet any applicable standard of conduct or have any particular belief, or that indemnification hereunder is otherwise not permitted.

(iv) **Defense to Indemnification and Burden of Proof.** It shall be a defense to any action brought by Indemnitee against the Company to enforce this Agreement (other than an action brought to enforce a claim for Losses incurred in defending against a Claim related to an Indemnifiable Event in advance of its final disposition by final adjudication to which there are no further rights of appeal) that it is not permissible under applicable law for the Company to indemnify Indemnitee for the amount claimed. In connection with any such action or any related Standard of Conduct Determination, the burden of proving such a defense or that Indemnitee did not satisfy the applicable standard of conduct shall be on the Company.

(v) **Resolution of Claims.** The Company acknowledges that a settlement or other disposition short of final judgment may be successful on the merits or otherwise for purposes of Section 8(a)(i) if it permits a party to avoid expense, delay, distraction, disruption and uncertainty. In the event that any Claim relating to an Indemnifiable Event to which Indemnitee is a party is resolved in any manner other than by adverse judgment against Indemnitee (including, without limitation, settlement of such action, claim or proceeding with our without payment of money or other consideration) it shall be presumed that Indemnitee has been successful on the merits or otherwise for purposes of Section 8(a)(i). The Company shall have the burden of proof to overcome this presumption.

9. Exclusions from Indemnification. Notwithstanding anything in this Agreement to the contrary, the Company shall not be obligated to:

(a) indemnify or advance funds to Indemnitee for Expenses or Losses with respect to proceedings initiated by Indemnitee, including any proceedings against the Company or its directors, officers, employees or other indemnitees and not by way of defense, except:

(i) proceedings referenced in Section 4 above (unless a court of competent jurisdiction determines that each of the material assertions made by Indemnitee in such proceeding was not made in good faith or was frivolous); or

(ii) where the Company has joined in or the Board has consented to the initiation of such proceedings;

(b) indemnify Indemnitee if a final decision by a court of competent jurisdiction determines that such indemnification is prohibited by applicable law;

(c) indemnify Indemnitee for the disgorgement of profits arising from the purchase or sale by Indemnitee of securities of the Company in violation of Section 16(b) of the Exchange Act, or any similar successor statute; or

(d) indemnify or advance funds to Indemnitee for Indemnitee's reimbursement to the Company of any bonus or other incentive-based or equity-based compensation previously received by Indemnitee or payment of any profits realized by Indemnitee from the sale of securities of the Company, as required in each case under the Exchange Act or other applicable law, including the listing requirements of any exchange on which the Company's securities are listed (including any such reimbursements under Section 304 of the Sarbanes-Oxley Act of 2002 in connection with an accounting restatement of the Company or the payment to the Company of profits arising from the purchase or sale by Indemnitee of securities in violation of Section 306 of the Sarbanes-Oxley Act) or by any Company plan or policy adopted pursuant to or in furtherance of, any of the foregoing.

10. Settlement of Claims. The Company shall not be liable to Indemnitee under this Agreement for any amounts paid in settlement of any threatened or pending Claim related to an Indemnifiable Event effected without the Company's prior written consent, which shall not be unreasonably withheld; provided, however, that if a Change in Control has occurred, the Company shall be liable for indemnification of Indemnitee for amounts paid in settlement if an Independent Counsel has approved the settlement. The Company shall not settle any Claim related to an Indemnifiable Event in any manner that would impose any Losses on Indemnitee without Indemnitee's prior written consent.

11. Duration. All agreements and obligations of the Company contained herein shall continue during the period that Indemnitee is a director or officer of the Company (or is serving at the request of the Company as a director, officer, employee, member, trustee or agent of another Enterprise) and shall continue thereafter (i) so long as Indemnitee may be subject to any possible Claim relating to an Indemnifiable Event (including any rights of appeal thereto) and (ii) throughout the pendency of any proceeding (including any rights of appeal thereto) commenced by Indemnitee to enforce or interpret his or her rights under this Agreement, even if, in either case, he or she may have ceased to serve in such capacity at the time of any such Claim or proceeding.

12. Non-Exclusivity. The rights of Indemnitee hereunder will be in addition to any other rights Indemnitee may have under the Constituent Documents, the General Corporation Law of the State of Delaware, any other contract or otherwise (collectively, "Other Indemnity Provisions"); provided, however, that (a) to the extent that Indemnitee otherwise would have any greater right to indemnification under any Other Indemnity Provision, Indemnitee will be deemed to have such greater right hereunder and (b) to the extent that any change is made to any Other Indemnity Provision which permits any greater right to indemnification than that provided under this Agreement as of the date hereof, Indemnitee will be deemed to have such greater right hereunder. Any prior indemnification agreements between the Company or any affiliated entity of the Company and the Indemnitee are hereby terminated and superseded by this Agreement.

13. Liability Insurance. For the duration of Indemnitee's service as a [director/officer] of the Company, and thereafter for so long as Indemnitee shall be subject to any pending Claim relating to an Indemnifiable Event, the Company shall use commercially reasonable efforts (taking into account the scope and amount of coverage available relative to the cost thereof) to continue to maintain in effect policies of directors' and officers' liability insurance providing coverage that

is at least substantially comparable in scope and amount to that provided by the Company's current policies of directors' and officers' liability insurance. In all policies of directors' and officers' liability insurance maintained by the Company, Indemnitee shall be named as an insured in such a manner as to provide Indemnitee the same rights and benefits as are provided to the most favorably insured of the Company's directors, if Indemnitee is a director, or of the

Company's officers, if Indemnitee is an officer (and not a director) by such policy. Upon request, the Company will provide to Indemnitee copies of all directors' and officers' liability insurance applications, binders, policies, declarations, endorsements and other related materials.

14. **No Duplication of Payments.** The Company shall not be liable under this Agreement to make any payment to Indemnitee in respect of any Losses to the extent Indemnitee has otherwise received payment under any insurance policy, the Constituent Documents, Other Indemnity Provisions or otherwise of the amounts otherwise indemnifiable by the Company hereunder.

15. **Subrogation.** In the event of payment to Indemnitee under this Agreement, the Company shall be subrogated to the extent of such payment to all of the rights of recovery of Indemnitee. Indemnitee shall execute all papers required and shall do everything that may be necessary to secure such rights, including the execution of such documents necessary to enable the Company effectively to bring suit to enforce such rights.

16. **Amendments.** No supplement, modification or amendment of this Agreement shall be binding unless executed in writing by both of the parties hereto. No waiver of any of the provisions of this Agreement shall be binding unless in the form of a writing signed by the party against whom enforcement of the waiver is sought, and no such waiver shall operate as a waiver of any other provisions hereof (whether or not similar), nor shall such waiver constitute a continuing waiver. Except as specifically provided herein, no failure to exercise or any delay in exercising any right or remedy hereunder shall constitute a waiver thereof.

17. **Binding Effect.** This Agreement shall be binding upon and inure to the benefit of and be enforceable by the parties hereto and their respective successors (including any direct or indirect successor by purchase, merger, consolidation or otherwise to all or substantially all of the business and/or assets of the Company), assigns, spouses, heirs and personal and legal representatives. The Company shall require and cause any successor (whether direct or indirect by purchase, merger, consolidation or otherwise) to all, substantially all or a substantial part of the business and/or assets of the Company, by written agreement in form and substance satisfactory to Indemnitee, expressly to assume and agree to perform this Agreement in the same manner and to the same extent that the Company would be required to perform if no such succession had taken place.

18. **Severability.** The provisions of this Agreement shall be severable in the event that any of the provisions hereof (including any portion thereof) are held by a court of competent jurisdiction to be invalid, illegal, void or otherwise unenforceable, and the remaining provisions shall remain enforceable to the fullest extent permitted by law. Upon such determination that any term or other provision is invalid, illegal or unenforceable, the parties hereto shall negotiate in good faith to modify this Agreement so as to effect the original intent of the parties as closely as possible in a mutually acceptable manner in order that the transactions contemplated hereby be

consummated as originally contemplated to the greatest extent possible.

19. **Notices.** All notices, requests, demands and other communications hereunder shall be in writing and shall be deemed to have been duly given if delivered by hand, against receipt, or mailed, by postage prepaid, certified or registered mail:

- (a) if to Indemnitee, to the address set forth on the signature page hereto.
- (b) if to the Company, to:

Rhythm Pharmaceuticals, Inc.
855 Boylston Street, 11th Floor
Boston, MA 02116
Attn: Chief Executive Officer

Notice of change of address shall be effective only when given in accordance with this Section. All notices complying with this Section shall be deemed to have been received on the date of hand delivery or on the third business day after mailing.

20. **Governing Law and Forum.** This Agreement shall be governed by and construed and enforced in accordance with the laws of the State of Delaware applicable to contracts made and to be performed in such state without giving effect to its principles of conflicts of laws. The Company and Indemnitee hereby irrevocably and unconditionally: (a) agree that any action or proceeding arising out of or in connection with this Agreement shall be brought only in the Delaware Court and not in any other state or federal court in the United States; (b) consent to submit to the exclusive jurisdiction of the Delaware Court for purposes of any action or proceeding arising out of or in connection with this Agreement; and (c) waive, and agree not to plead or make, any claim that the Delaware Court lacks venue or that any such action or proceeding brought in the Delaware Court has been brought in an improper or inconvenient forum.

21. **Headings.** The headings of the sections and paragraphs of this Agreement are inserted for convenience only and shall not be deemed to constitute part of this Agreement or to affect the construction or interpretation thereof.

22. **Counterparts.** This Agreement may be executed in one or more counterparts, each of which shall for all purposes be deemed to be an original, but all of which together shall constitute one and the same Agreement.

[SIGNATURE PAGE FOLLOWS]

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the date first above written.

By: _____

Name:

Title:

INDEMNITEE

Name:

Address:

RHYTHM PHARMACEUTICALS, INC.

2017 EQUITY INCENTIVE PLAN

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RHYTHM PHARMACEUTICALS, INC.

2017 EQUITY INCENTIVE PLAN

1. Purpose

This Plan is intended to provide incentives that will attract, retain and motive highly competent officers, directors, employees, consultants and advisors to promote the success of the Company's business and align employees' interests with stockholders' interests. The Plan is intended to be an incentive stock option plan within the meaning of Section 422 of the Code, but not all Awards are required to be Incentive Options.

This Plan serves as the successor to the Company's 2015 Equity Incentive Plan (the "Predecessor Plan"), and no further awards shall be made under the Predecessor Plan on or after the Effective Date. All awards outstanding under the Predecessor Plan on the Effective Date shall be transferred to this Plan and shall be treated as outstanding under this Plan. However, each outstanding award so transferred shall continue to be governed solely by the terms of the documents evidence such award, and no provision of the Plan shall be deemed to affect or modified the rights or obligations of the holders of such transferred awards. This Plan and all definitions hereunder shall be interpreted consistent with the foregoing.

2. Definitions

As used in this Plan, the following terms shall have the respective meanings set out below, unless the context clearly requires otherwise:

2.1. **Accelerate, Accelerated, and Acceleration**, means: (a) when used with respect to an Option or Stock Appreciation Right, that as of the time of reference such Option or Stock Appreciation Right will become exercisable with respect to some or all of the shares of Stock for which it was not then otherwise exercisable by its terms; (b) when used with respect to Restricted Stock or Restricted Stock Units, that the Risk of Forfeiture otherwise applicable to such Restricted Stock or Restricted Stock Units shall expire with respect to some or all of such shares of Restricted Stock or such Restricted Stock Units

then still otherwise subject to the Risk of Forfeiture; and (c) when used with respect to Performance Units, that the applicable Performance Goals or other business objectives shall be deemed to have been met as to some or all of such Performance Units.

2.2. Affiliate means any parent or subsidiary corporation of the Company (within the meaning of Sections 424(e) and 424(f) of the Code, respectively).

2.3. Award means any grant or sale pursuant to the Plan or award outstanding under the Predecessor Plan as of the Effective Date of Options, Stock Appreciation Rights, Performance Units, Restricted Stock, Restricted Stock Units, Stock Grants or any of the foregoing intended to constitute Qualified Performance-Based Awards.

2.4. Award Agreement means an agreement between the Company and the recipient of an Award, or other notice of grant of an Award, setting forth the terms and conditions of the Award.

2.5. Board means the Company's Board of Directors.

2.6. Change of Control means the occurrence of any of the following after the date of the approval of the Plan by the Board:

(a) a Transaction (as defined in Section 8.4), unless securities possessing more than 50% of the total combined voting power of the survivor's or acquiror's outstanding securities (or the securities of any parent thereof) are held by a person or persons who held securities possessing more than 50% of the total combined voting power of the Company's outstanding securities immediately prior to that Transaction; or

(b) any person or group of persons (within the meaning of Section 13(d)(3) of the Securities Exchange Act of 1934, as amended and in effect from time to time) that, directly or indirectly, acquires, including but not limited to by means of a merger or consolidation, beneficial ownership (determined pursuant to Securities and Exchange Commission Rule 13d-3 promulgated under the said Exchange Act) of securities possessing more than 50% of the total combined voting power of the Company's outstanding securities unless pursuant to a tender or exchange offer made directly to the Company's stockholders that the Board recommends such stockholders accept, other than (i) the Company or any of its Affiliates, (ii) an employee benefit plan of the Company or any of its Affiliates, (iii) a trustee or other fiduciary holding securities under an employee benefit plan of the Company or any of its Affiliates, or (iv) an underwriter temporarily holding securities pursuant to an offering of such securities; or

(c) over a period of thirty-six (36) consecutive months or less, there is a change in the composition of the Board such that a majority of the Board members (rounded up to the next whole number, if a fraction) ceases, by reason of one or more proxy contests for the election of Board members, to be composed of individuals who either (i) have been Board members continuously since the beginning of that period, or (ii) have been elected or nominated for election as Board members during such period by at least a majority of the Board members described in the preceding clause (i) who were still in office at the time that election or nomination was approved by the Board; or

(d) a majority of the Board votes in favor of a decision that a Change of Control has occurred, which vote may be adopted by the Board with the intention that such vote become effective subject to and contingent upon the occurrence of certain events, in which case such Change of Control shall not be deemed to have occurred unless and until such vote becomes effective in accordance with its terms.

2.7. Code means the Internal Revenue Code of 1986, as amended from time to time, or any successor statute thereto, and any regulations issued from time to time thereunder.

2.8. Committee means the Compensation Committee of the Board, which in general is responsible for the administration of the Plan, as provided in Section 5 of this Plan. For any period during which no such committee is in existence "Committee" shall mean the Board and all authority and responsibility assigned to the Committee under the Plan shall be exercised, if at all, by the Board.

2.9. Company means Rhythm Pharmaceuticals, Inc., a corporation organized under the laws of the State of Delaware.

2.10. "Forfeiture," "forfeit," and derivations thereof, when used in respect of Restricted Stock purchased by a Participant, includes the Company's repurchase of such Restricted Stock at less than its then Market Value as a means intended to effect a forfeiture of value.

2.11. Grant Date means the date as of which an Option is granted, as determined under Section 7.1(a).

2.12. Incentive Option means an Option which by its terms is to be treated as an "incentive stock option" within the meaning of Section 422 of the Code.

2.13. Market Value means the value of a share of Stock on a particular date determined by such methods or procedures as may be established by the Committee. Unless otherwise determined by the Committee, the Market Value of Stock as of any date is the closing price for the Stock as reported on the Nasdaq Stock Market (or on any other national securities exchange on which the Stock is then listed) for that date or, if no closing price is reported for that date, the closing price on the first following date for which a closing price is reported. For purposes of Awards effective as of the effective date of the Company's initial public offering, Market Value of Stock shall be the price at which the Company's Stock is offered to the public in its initial public offering.

2.14. Nonstatutory Option means any Option that is not an Incentive Option.

2.15. Option means an option to purchase shares of Stock.

2.16. Optionee means an eligible individual to whom an Option shall have been granted under the Plan.

2.17. Participant means any holder of an outstanding Award under the Plan or the Predecessor Plan.

2.18. Performance Criteria and Performance Goals have the meanings given such terms in Section 7.7(f).

2.19. Performance Period means one or more periods of time, which may be of varying and overlapping durations, selected by the Committee, over which the attainment of one or more Performance Goals or other business objectives will be measured for purposes of determining a Participant's right to, and the payment of, an Award.

2.20. Performance Unit means a right granted to a Participant under Section 7.5, to receive cash, Stock or other Awards, the payment of which is contingent on achieving Performance Goals or other business objectives established by the Committee.

2.21. Plan means this 2017 Equity Incentive Plan of the Company, as amended from time to time, and including any attachments or addenda hereto.

2.22. Qualified Performance-Based Awards means Awards intended to qualify as "performance-based compensation" under Section 162(m) of the Code.

2.23. Restricted Stock means a grant or sale of shares of Stock to a Participant subject to a Risk of Forfeiture.

2.24. Restricted Stock Units means rights to receive shares of Stock, cash or other Awards at the close of a Restriction Period, subject to a Risk of Forfeiture.

2.25. Restriction Period means the period of time, established by the Committee in connection with an Award of Restricted Stock or Restricted Stock Units, during which the shares of Restricted Stock or Restricted Stock Units are subject to a Risk of Forfeiture described in the applicable Award Agreement.

2.26. Risk of Forfeiture means a limitation on the right of the Participant to retain Restricted Stock or Restricted Stock Units, including a right of the Company to reacquire shares of Restricted Stock at less than their then Market Value, arising because of the occurrence or non-occurrence of specified

events or conditions.

2.27. Stock means common stock, par value \$0.001 per share, of the Company, and such other securities as may be substituted for such common stock pursuant to Section 8.

2.28. Stock Appreciation Right means a right to receive any excess in the Market Value of shares of Stock (except as otherwise provided in Section 7.2(c)) over a specified exercise price.

2.29. Stock Grant means the grant of shares of Stock not subject to restrictions or other forfeiture conditions.

2.30. Stockholders' Agreement means any agreement by and among the holders of at least a majority of the outstanding voting securities of the Company and setting forth, among other provisions, restrictions upon the transfer of shares of Stock or on the exercise of rights appurtenant thereto (including but not limited to voting rights).

2.31. Ten Percent Owner means a person who owns, or is deemed within the meaning of Section 422(b)(6) of the Code to own, stock possessing more than 10% of the total combined voting power of all classes of stock of the Company (or any parent or subsidiary corporations of the Company, as defined in Sections 424(e) and (f), respectively, of the Code). Whether a person is a Ten Percent Owner shall be determined with respect to an Option based on the facts existing immediately prior to the Grant Date of the Option.

3. **Term of the Plan**

The Plan became effective on October , 2017 upon consummation of the Company's initial public offering (the "Effective Date") and, unless earlier terminated by the Committee, shall terminate on October , 2027. Awards granted pursuant to the Predecessor Plan or to the Plan within that period shall not expire solely by reason of the termination of the Plan.

4. **Stock Subject to the Plan**

4.1. Plan Share Limitations.

(a) Limitation. The maximum number of shares of Stock that may be issued pursuant to or subject to outstanding Awards granted under the Plan shall not exceed 4,018,538 shares of Stock. Such share reserve includes 495,759 shares of Stock available for issuance under the Predecessor Plan as of the Effective Date, including the portion of those shares subject to Options outstanding under the Predecessor Plan as of the Effective Date, plus an additional 3,522,779 shares. Notwithstanding the foregoing, however, beginning on the first January 1 following consummation of the Company's initial public offering, the number of shares of Stock authorized under the first sentence of this Section 4.1(a) of the Plan will be increased each January 1 by an amount equal to four percent (4%) of outstanding shares of Stock as of the end of the immediately preceding fiscal year. Notwithstanding the foregoing, the Board may act prior to January 1 of a given year to provide that there will be no such January 1 increase in the number of shares of Stock authorized under this Section 4.1(a) of the Plan for such year or that the increase in the number of shares of Stock authorized under this Section 4.1(a) of the Plan for such year will be a lesser number than would otherwise occur pursuant to the preceding sentence. Notwithstanding

the preceding sentences, in no event shall the number of shares available for issuance pursuant to Incentive Options over the term of the Plan exceed 4,018,583 shares of Stock.

(b) **Application.** For purposes of applying the foregoing limitation of Section 4.1(a), (i) if any Option or Stock Appreciation Right expires, terminates, or is cancelled for any reason without having been exercised in full, or if any other Award is forfeited, the shares of Stock not purchased by the holder or subject to Awards which are forfeited, as the case may be, shall again be available for Awards to be granted under the Plan, (ii) if any Option is exercised by delivering previously owned shares of Stock or the withholding of a portion of the otherwise issuable shares of Stock subject to the Option in payment of the exercise price therefor, only the net number of shares, that is, the number of shares of Stock issued minus the number received by the Company in payment of the exercise price, shall be considered to have been issued pursuant to an Award granted under the Plan, and (iii) any shares of Stock either delivered to or withheld by the Company in satisfaction of tax withholding obligations of the Company or an Affiliate with respect to an Award shall again be available for Awards to be granted under the Plan. In addition, settlement of any Award shall not count against the foregoing limitations except to the extent settled in the form of Stock. For the avoidance of doubt, Awards outstanding under the Predecessor Plan shall be treated consistent with Awards granted under this Plan for all purposes, including for purposes of this Section 4.1(b). Shares of Stock issued pursuant to the Plan may be either authorized but unissued shares or shares held by the Company in its treasury.

4.2. **Per Person Limitations.** The maximum number of shares of Stock that may be subject to Options or Stock Appreciation Rights or any combination thereof granted to any one Participant during any single calendar year shall be 1,200,000. The maximum number of shares of Stock that may be subject to all other Awards or any combination thereof granted to any one Participant during any single calendar year that are intended to be Qualified Performance-Based Awards shall be 1,200,000. The maximum value of awards denominated in cash granted to any one person, other than a non-employee member of the Board, during any single calendar year and that are intended to be Qualified Performance-Based Awards shall be \$30,000,000. Each of the foregoing limitations shall be doubled with respect to awards granted to an individual during the first calendar year in which he or she commences employment. The per Participant limits described in this Section 4.2 shall be construed and applied consistent with Section 162(m) of the Code.

4.3. **Limitations on Grants to Non-Employee Board Members.** The maximum value of awards denominated in cash granted to any non-employee member of the Board, during any single calendar year shall be \$1,000,000. For purposes of this limitation, the value of an award shall be the grant date fair value of the award (as determined for the Company's financial statements).

4.4. **Adjustment of Limitations.** Each of the share limitations of this Section 4 shall be subject to adjustment pursuant to Section 8 of the Plan, but in the case of the limitations of Section 4.2, only if and to the extent consistent with Section 162(m) of the Code.

5. Administration

The Plan shall be administered by the Committee; provided, however, that at any time and on any one or more occasions the Board may itself exercise any of the powers and responsibilities assigned the Committee under the Plan and when so acting shall have the benefit of all of the provisions of the Plan pertaining to the Committee's exercise of its authorities hereunder; and provided further, however, that the Committee may delegate to an executive officer or officers the authority to grant Awards hereunder to employees who are not executive officers, and to consultants, up to such maximum number and in accordance with such other guidelines as the Committee shall specify by resolution at any time or from time to time. To the extent required by applicable law, any such delegation may not include the authority

to grant Restricted Stock, unless the delegate is a committee of the Board, including a committee consisting solely of an executive officer who is a Board member. Subject to the provisions of the Plan, the Committee shall have complete authority, in its discretion, to make or to select the manner of making all determinations with respect to each Award to be granted by the Company under the Plan including the officer, employee, consultant, advisor or director to receive the Award and the form of Award. In making such determinations, the Committee may take into account the nature of the services rendered by the respective officers, employees, consultants, advisors and directors, their present and potential contributions to the success of the Company and its Affiliates, and such other factors as the Committee in its discretion shall deem relevant. Subject to the provisions of the Plan, the Committee shall also have complete authority to interpret the Plan, to prescribe, amend and rescind rules and regulations relating to it, to determine the terms and provisions of the respective Award Agreements (which need not be identical), and to make all other determinations necessary or advisable for the administration of the Plan. The Committee's determinations made in good faith on matters referred to in the Plan shall be final, binding and conclusive on all participants, beneficiaries, heirs, assigns or other persons having or claiming any interest under the Plan or an Award made pursuant hereto.

6. Authorization of Grants

6.1. **Eligibility.** The Committee may grant from time to time and at any time prior to the termination of the Plan one or more Awards, either alone or in combination with any other Awards, to any officer or employee of or consultant or advisor to one or more of the Company and its Affiliates or to any non-employee member of the Board or of any board of directors (or similar governing authority) of any Affiliate. However, only employees of the Company and its Affiliates shall be eligible for the grant of an Incentive Option.

6.2. **General Terms of Awards.** Each grant of an Award shall be subject to all applicable terms and conditions of the Plan (including but not limited to any specific terms and conditions applicable to that type of Award set out in the following Section), and such other terms and conditions, not inconsistent with the terms of the Plan, as the Committee may prescribe. No prospective Participant shall have any rights with respect to an Award, unless and until such Participant shall have complied with the applicable terms and conditions of such Award (including if applicable delivering a fully executed copy of any agreement evidencing an Award to the Company).

6.3. **Effect of Termination of Employment, Etc.** Unless the Committee shall provide otherwise with respect to any Award (including, but not limited to, in a Participant's Award Agreement), if the Participant's employment or other association with the Company and its Affiliates ends for any reason, including because of the Participant's employer ceasing to be an Affiliate, (a) any outstanding Option or Stock Appreciation Right of the Participant shall cease to be exercisable in any respect not later than ninety (90) days following that event and, for the period it remains exercisable following that event, shall be exercisable only to the extent exercisable at the date of that event, and (b) any other outstanding Award of the Participant to the extent that it is then still subject to Risk of Forfeiture shall be forfeited or otherwise subject to return to or repurchase by the Company on the terms specified in the applicable Award Agreement. Cessation of the performance of services in one capacity, for example, as an employee, shall not result in termination of an Award while the Participant continues to perform services in another capacity, for example as a director. Military or sick leave or other bona fide leave approved by the Company shall not be deemed a termination of employment or other association; *provided*, however, that should such leave exceed three (3) months, then for

purposes of determining the period within which an Incentive Option may be exercised as such under the federal tax laws, the Participant's service shall be deemed to cease on the first day immediately following the expiration of such three (3)-month period, unless the Participant is provided with the right to return to employment following such leave either by statute or by written contract. To the extent consistent with applicable law, the Committee may provide

that Awards continue to vest for some or all of the period of any such leave, or that their vesting shall be tolled during any such leave and only recommence upon the Participant's return from leave, if ever.

6.4. Non-Transferability of Awards. Except as otherwise provided in this Section 6.4, Awards shall not be transferable, and no Award or interest therein may be sold, transferred, pledged, assigned, or otherwise alienated or hypothecated, other than by will or by the laws of descent and distribution. The provisions of the immediately preceding sentence shall not be applicable to Stock Grants which shall not be subject to any transfer restrictions under this Section 6.4. All of a Participant's rights in any Award may be exercised during the life of the Participant only by the Participant or the Participant's legal representative. However, the Committee may, at or after the grant of an Award of a Nonstatutory Option, or shares of Restricted Stock, provide that such Award may be transferred by the recipient to a family member; *provided, however,* that any such transfer is without payment of any consideration whatsoever and that no transfer shall be valid unless first approved by the Committee, acting in its sole discretion. For this purpose, "family member" means any child, stepchild, grandchild, parent, grandparent, stepparent, spouse, former spouse, sibling, niece, nephew, mother-in-law, father-in-law, son-in-law, daughter-in-law, brother-in-law, or sister-in-law, including adoptive relationships, any person sharing the employee's household (other than a tenant or employee), a trust in which the foregoing persons have more than fifty (50) percent of the beneficial interests, a foundation in which the foregoing persons (or the Participant) control the management of assets, and any other entity in which these persons (or the Participant) own more than fifty (50) percent of the voting interests.

7. Specific Terms of Awards

7.1. Options.

- (a) Date of Grant. The granting of an Option shall take place at the time specified in the Award Agreement.
- (b) Exercise Price. The price at which shares of Stock may be acquired under each Option shall be not less than 100% of the Market Value of Stock on the Grant Date, or for an Incentive Option not less than 110% of the Market Value of Stock on the Grant Date if the Optionee is a Ten Percent Owner.
- (c) Option Period. No Incentive Option may be exercised on or after the tenth (10th) anniversary of the Grant Date, or on or after the fifth (5th) anniversary of the Grant Date if the Optionee is a Ten Percent Owner. The Option period under each Nonstatutory Option shall not be so limited solely by reason of this Section.

(d) Exercisability. An Option may be immediately exercisable or become exercisable in such installments, cumulative or non-cumulative, as the Committee may determine. In the case of an Option not otherwise immediately exercisable in full, the Committee may Accelerate such Option in whole or in part at any time; *provided, however,* that in the case of an Incentive Option, any such Acceleration of the Option would not cause the Option to fail to comply with the provisions of Section 422 of the Code or the Optionee consents to the Acceleration.

(e) Method of Exercise. An Option may be exercised by the Optionee giving written notice, in the manner provided in Section 17, specifying the number of shares of Stock with respect to which the Option is then being exercised. The notice shall be accompanied by payment in the form of cash or check payable to the order of the Company in an amount equal to the exercise price of the shares of Stock to be purchased or, subject in each instance to the Committee's approval, acting in its sole discretion, and to such conditions, if any, as the Committee may deem necessary to avoid adverse

accounting effects to the Company,

- (i) by delivery to the Company of shares of Stock having a Market Value equal to the exercise price of the shares to be purchased, or
- (ii) by the Company withholding shares of Stock otherwise issuable under the Option with such withheld shares having an aggregate Market Value equal to the aggregate exercise price of the shares to be purchased, or
- (iii) unless prohibited by applicable law, by delivery to the Company of the Optionee's executed promissory note in the principal amount equal to the exercise price of the shares of Stock to be purchased and otherwise in such form as the Committee shall have approved.

If the Stock is traded on an established market, payment of any exercise price may also be made through and under the terms and conditions of any formal cashless exercise program authorized by the Company entailing the sale of the Stock subject to an Option in a brokered transaction (other than to the Company). Receipt by the Company of such notice and payment in any authorized or combination of authorized means shall constitute the exercise of the Option. Within thirty (30) days thereafter but subject to the remaining provisions of the Plan, the Company shall deliver or cause to be delivered to the Optionee or his agent a certificate or certificates or shall cause the Stock to be held in book-entry position through the direct registration system of the Company's transfer agent for the number of shares then being purchased. Such shares of Stock shall be fully paid and nonassessable.

(f) Limit on Incentive Option Characterization. An Incentive Option shall be considered to be an Incentive Option only to the extent that the number of shares of Stock for which the Option first becomes exercisable in a calendar year do not have an aggregate Market Value (as of the date of the grant of the Option) in excess of the "current limit". Except to the extent otherwise provided under applicable law or regulation, the current limit for any Optionee for any calendar year shall be \$100,000 minus the aggregate Market Value at the date of grant of the number of shares of Stock available for purchase for the first time in the same year under each other Incentive Option previously granted to the Optionee under the Plan, and under each other incentive stock option previously granted to the Optionee under any other incentive stock option plan of the Company and its parent and subsidiary

corporations (as defined in Sections 424(e) and (f) of the Code). Any shares of Stock which would cause the foregoing limit to be violated shall be deemed to have been granted under a separate Nonstatutory Option, otherwise identical in its terms to those of the Incentive Option.

(g) Notification of Disposition. Each person exercising any Incentive Option granted under the Plan shall be deemed to have covenanted with the Company to report to the Company any disposition of the shares of Stock issued upon such exercise prior to the expiration of the holding periods specified by Section 422(a)(1) of the Code and, if and to the extent that the realization of income in such a disposition imposes upon the Company federal, state, local or other withholding tax requirements, or any such withholding is required to secure for the Company an otherwise available tax deduction, to remit to the Company an amount in cash sufficient to satisfy those requirements.

7.2. Stock Appreciation Rights.

(a) Tandem or Stand-Alone. Stock Appreciation Rights may be granted in tandem with an Option (at or, in the case of a Nonstatutory Option, after, the award of the Option), or alone and unrelated to an Option. Stock Appreciation Rights in tandem with an Option shall terminate to the extent that the related Option is exercised, and the related Option shall terminate to the extent that the tandem

Stock Appreciation Rights are exercised.

(b) Exercise Price. Stock Appreciation Rights shall have an exercise price of not less than one hundred percent (100%) of the Market Value of the Stock on the date of award, or in the case of Stock Appreciation Rights in tandem with Options, the exercise price of the related Option.

(c) Other Terms. Except as the Committee may deem inappropriate or inapplicable in the circumstances, Stock Appreciation Rights shall be subject to terms and conditions substantially similar to those applicable to a Nonstatutory Option. In addition, a Stock Appreciation Right related to an Option which can only be exercised during limited periods following a Change of Control may entitle the Participant to receive an amount based upon the highest price paid or offered for Stock in any transaction relating to the Change of Control or paid during the thirty (30) day period immediately preceding the occurrence of the Change of Control in any transaction reported in the stock market in which the Stock is normally traded.

7.3. Restricted Stock.

(a) Purchase Price. Shares of Restricted Stock shall be issued under the Plan for such consideration, if any, in cash, other property or services, or any combination thereof, as is determined by the Committee.

(b) Issuance of Stock. Each Participant receiving a Restricted Stock Award, subject to subsection (c) below, shall be issued a stock certificate in respect of such shares of Restricted Stock or the shares shall be held in book-entry position through the direct registration system of the Company's transfer agent. If a certificate is issued, such certificate shall be registered in the name of such Participant, and, if applicable, shall bear an appropriate legend referring to the terms, conditions, and restrictions applicable to such Award substantially in the following form:

"The shares evidenced by this certificate are subject to the terms and conditions of Rhythm Pharmaceuticals, Inc.'s 2017 Equity Incentive Plan and an Award Agreement entered into by the registered owner and Rhythm Pharmaceuticals, Inc., copies of which will be furnished by the Company to the holder of the shares evidenced by this certificate upon written request and without charge."

If the Stock is in book-entry position through the direct registration system of the Company's transfer agent, the restrictions will be appropriately noted.

(c) Escrow of Shares. The Committee may require that any stock certificates evidencing shares of Restricted Stock be held in custody by a designated escrow agent (which may but need not be the Company) until the restrictions thereon shall have lapsed, and that the Participant deliver a stock power, endorsed in blank, relating to the Stock covered by such Award.

(d) Restrictions and Restriction Period. During the Restriction Period applicable to shares of Restricted Stock, such shares shall be subject to limitations on transferability and a Risk of Forfeiture arising on the basis of such conditions related to the performance of services, Company or Affiliate performance or otherwise as the Committee may determine and provide for in the applicable Award Agreement. Any such Risk of Forfeiture may be waived or terminated, or the Restriction Period shortened, at any time by the Committee on such basis as it deems appropriate.

(e) Rights Pending Lapse of Risk of Forfeiture or Forfeiture of Award. Except as otherwise provided in the Plan or the applicable Award Agreement, the Participant shall have all of the

rights of a stockholder of the Company with respect to any outstanding shares of Restricted Stock, including the right to vote, and the right to receive any dividends with respect to, the shares of Restricted Stock (but any dividends or other distributions payable in shares of Stock or other securities of the Company shall constitute additional Restricted Stock, subject to the same Risk of Forfeiture as the shares of Restricted Stock in respect of which such shares of Stock or other securities are paid). The Committee, as determined at the time of Award, may permit or require the payment of cash dividends to be deferred and, if the Committee so determines, reinvested in additional Restricted Stock to the extent shares of Stock are available under Section 4.

(f) Lapse of Restrictions. If and when the Restriction Period expires without a prior forfeiture, any certificates for such shares shall be delivered to the Participant promptly if not theretofore so delivered.

7.4. Restricted Stock Units.

(a) Character. Subject to Section 10, each Restricted Stock Unit shall entitle the recipient to a share of Stock at a close of such Restriction Period as the Committee may establish and subject to a Risk of Forfeiture arising on the basis of such conditions relating to the performance of

services, Company or Affiliate performance or otherwise as the Committee may determine and provide for in the applicable Award Agreement. Any such Risk of Forfeiture may be waived or terminated, or the Restriction Period shortened, at any time by the Committee on such basis as it deems appropriate.

(b) Form and Timing of Payment. Payment of earned Restricted Stock Units shall be made promptly following the close of the applicable Restriction Period. At the discretion of the Committee, Participants may be entitled to receive payments equivalent to any dividends declared with respect to Stock referenced in grants of Restricted Stock Units but only following the close of the applicable Restriction Period and then only if the underlying Stock shall have been earned. Unless the Committee shall provide otherwise, any such dividend equivalents shall be paid, if at all, without interest or other earnings. The Committee may permit or, if it so provides at grant require, a Participant to defer such Participant's receipt of the payment that would otherwise be due to such Participant with respect to Restricted Stock Units. If any such deferral election is required or permitted, the Committee shall establish rules and procedures for such payment deferrals.

7.5. Performance Units.

(a) Character. Each Performance Unit shall entitle the recipient to the value of a specified number of shares of Stock, over the initial value for such number of shares, if any, established by the Committee at the time of grant, at the close of a specified Performance Period to the extent specified business objectives, including but not limited to Performance Goals, shall have been achieved.

(b) Earning of Performance Units. The Committee shall set Performance Goals or other business objectives in its discretion which, depending on the extent to which they are met within the applicable Performance Period, will determine the number and value of Performance Units that will be paid out to the Participant. After the applicable Performance Period has ended, the holder of Performance Units shall be entitled to receive payout on the number and value of Performance Units earned by the Participant over the Performance Period, to be determined as a function of the extent to which the corresponding Performance Goals or other business objectives have been achieved.

(c) Form and Timing of Payment. Unless otherwise provided in the applicable Award Agreement, payment of earned Performance Units shall be made in a single lump sum following the close of the applicable Performance Period. At the discretion of the Committee, Participants may be

entitled to receive any dividends declared with respect to Stock which have been earned in connection with grants of Performance Units which have been earned, but not yet distributed to Participants. The Committee may permit or, if it so provides at grant require, a Participant to defer such Participant's receipt of the payment of cash or the delivery of Stock that would otherwise be due to such Participant by virtue of the satisfaction of any requirements or goals with respect to Performance Units. If any such deferral election is required or permitted, the Committee shall establish rules and procedures for such payment deferrals.

7.6. Stock Grants. Stock Grants shall be awarded solely in recognition of significant prior or expected contributions to the success of the Company or its Affiliates, as an inducement to employment, in lieu of compensation otherwise already due and in such other limited circumstances as the Committee deems appropriate. Stock Grants shall be made without forfeiture conditions of any kind.

7.7. Qualified Performance-Based Awards.

(a) Purpose. The purpose of this Section 7.7 is to provide the Committee the ability to qualify Awards as "performance-based compensation" under Section 162(m) of the Code. If the Committee, in its discretion, decides to grant an Award as a Qualified Performance-Based Award, the provisions of this Section 7.7 will control over any contrary provision contained in the Plan. In the course of granting any Award, the Committee may specifically designate the Award as intended to qualify as a Qualified Performance-Based Award. However, no Award shall be considered to have failed to qualify as a Qualified Performance-Based Award solely because the Award is not expressly designated as a Qualified Performance-Based Award, if the Award otherwise satisfies the provisions of this Section 7.7 and the requirements of Section 162(m) of the Code applicable to "performance-based compensation."

(b) Authority. All grants of Awards intended to qualify as Qualified Performance-Based Awards and the determination of the terms applicable thereto shall be made by the Committee. If not all of the members thereof qualify as "outside directors" within the meaning of Section 162 of the Code, however, all grants of Awards intended to qualify as Qualified Performance-Based Awards and the determination of the terms applicable thereto shall be made by a subcommittee of the Committee consisting of such of the members of the Committee as do so qualify. Any reference in this Section 7.7 to the Committee shall mean any such subcommittee if required under the preceding sentence, and any action by such a subcommittee shall be considered the action of the Committee for purposes of the Plan.

(c) Discretion of Committee with Respect to Qualified Performance-Based Awards. Any form of Award permitted under the Plan, other than a Stock Grant, may be granted as a Qualified Performance-Based Award. Options and Stock Appreciation Rights may be granted as Qualified Performance-Based Awards in accordance with Section 7.1 and Section 7.2, respectively, except that the Option or Stock Appreciation Right may become exercisable based on continued service, on satisfaction of Performance Goals or other business objectives, or on a combination thereof. Each other Award intended to qualify as a Qualified Performance-Based Award, such as Restricted Stock, Restricted Stock Units, or Performance Units, shall be subject to satisfaction of one or more Performance Goals except as otherwise provided in this Section 7.7. The Committee will have full discretion to select the length of any applicable Restriction Period or Performance Period, the kind and/or level of the applicable Performance Goal, and whether the Performance Goal is to apply to the Company, a subsidiary of the Company or any division or business unit or to the individual. Any Performance Goal or Goals applicable to Qualified Performance-Based Awards shall be objective, shall be established not later than ninety (90) days after the beginning of any applicable Performance Period (or at such other date as may be required or permitted for "performance-based compensation" under Section 162(m) of the Code) and shall otherwise meet the requirements of Section 162(m) of the Code, including the requirement that the outcome of the Performance Goal or Goals be substantially uncertain (as defined for purposes of Section 162(m) of the

(d) **Payment of Qualified Performance-Based Awards.** A Participant will be eligible to receive payment under a Qualified Performance-Based Award which is subject to achievement of a Performance Goal or Goals only if the applicable Performance Goal or Goals are achieved within the applicable Performance Period, as determined by the Committee, *provided*, that a Qualified Performance-Based Award may be deemed earned as a result of death, becoming disabled, or in connection with a change of control (within the meaning of Section 162(m) of the Code) if otherwise provided in the Plan or the applicable Award Agreement even if the Award would not constitute “performance-based compensation” under Section 162(m) of the Code following the occurrence of such an event. In determining the actual size of an individual Qualified Performance-Based Award, the Committee may reduce or eliminate the amount of the Qualified Performance-Based Award earned for the Performance Period, if in its sole and absolute discretion, such reduction or elimination is appropriate.

(e) **Limitation on Adjustments for Certain Events.** No adjustment of any Qualified Performance-Based Award pursuant to Section 8 shall be made except on such basis, if any, as will not cause such Award to provide other than “performance-based compensation” within the meaning of Section 162(m) of the Code.

(f) **Definitions.** For purposes of the Plan

(i) **Performance Criteria** means the criteria that the Committee selects for purposes of establishing the Performance Goal or Performance Goals for a Participant for a Performance Period. The Performance Criteria used to establish Performance Goals are limited to: (i) net earnings (either before or after one or more of (A) interest, (B) taxes, (C) depreciation and (D) amortization), (ii) gross or net sales or revenue, (iii) net income (either before or after taxes), (iv) adjusted net income, (v) operating earnings or profit, (vi) cash flow (including, but not limited to, operating cash flow and free cash flow), (vii) return on assets, (viii) return on capital, (ix) return on stockholders’ equity, (x) total stockholder return, (xi) return on sales, (xii) gross or net profit or operating margin, (xiii) costs, (xiv) expenses, (xv) working capital, (xvi) earnings per share, (xvii) adjusted earnings per share, (xviii) price per share, (xix) regulatory body approval for commercialization of a product, (xx) implementation, completion or attainment of objectives relating to research, development, regulatory, commercial, or strategic milestones or developments; (xxi) market share, (xxii) economic value, (xxiii) revenue, (xxiv) revenue growth and (xxv) operational and organizational metrics.

(ii) **Performance Goals** means, for a Performance Period, the written goal or goals established by the Committee for the Performance Period based upon one or more of the Performance Criteria. The Performance Goals may be expressed in terms of overall Company performance or the performance of a division, business unit, subsidiary, or an individual, either individually, alternatively or in any combination, applied to either the Company as a whole or to a business unit or Affiliate, either individually, alternatively or in any combination, and measured either quarterly, annually or cumulatively over a period of years, on an absolute basis or relative to a pre-established target, to previous years’ results or to a designated comparison group, in each case as specified by the Committee. The Committee will objectively define the manner of calculating the Performance Goal or Goals it selects to use for such Performance Period for such Participant, including whether or to what extent there shall not be taken into account any of the following events that occurs during a Performance Period: (i) asset

write-downs, (ii) litigation, claims, judgments or settlements, (iii) the effect of changes in tax law, accounting principles or other such laws or provisions affecting reported results, (iv) accruals for reorganization and restructuring programs and (v) any extraordinary, unusual, non-recurring or non-comparable items (A) as described in Accounting Standard Codification Section 225-20, (B) as described in management’s discussion and analysis of financial condition and results of operations appearing in the Company’s Annual Report to stockholders for the applicable year, or (C) publicly announced by the Company in a press release or conference call relating to the Company’s results of operations or financial condition for a completed quarterly or annual fiscal period.

7.8. **Awards to Participants Outside the United States.** The Committee may modify the terms of any Award under the Plan granted to a Participant who is, at the time of grant or during the term of the Award, resident or primarily employed outside of the United States in any manner deemed by the Committee to be necessary or appropriate in order that the Award shall conform to laws, regulations, procedures, and customs of the country in which the Participant is then resident or primarily employed, or so that the value and other benefits of the Award to the Participant, as affected by foreign tax laws and other restrictions applicable as a result of the Participant’s residence or employment abroad, shall be as comparable as practicable to the value of such an Award to a Participant who is resident or primarily employed in the United States. The Committee may establish supplements or sub-plans to, or amendments, restatements, or alternative versions of, the Plan for the purpose of granting and administrating any such modified Award. No such modification, supplement, sub-plan, amendment, restatement or alternative version may increase the share limit of Section 4.

8. Adjustment Provisions

8.1. **Adjustment for Corporate Actions.** All of the share numbers set forth in the Plan reflect the capital structure of the Company as of the Effective Date. If subsequent to that date the outstanding shares of Stock (or any other securities covered by the Plan by reason of the prior application of this Section) are increased, decreased, or exchanged for a different number or kind of shares or other securities, or if additional shares or new or different shares or other securities are distributed with respect to shares of Stock, as a result of a reorganization, recapitalization, reclassification, stock dividend, stock split, reverse stock split, or other similar distribution with respect to such shares of Stock, an equitable adjustment will be made in (i) the maximum numbers and kinds of shares provided in Section 4, (ii) the numbers and kinds of shares or other securities subject to the then outstanding Awards, (iii) the exercise price for each share or other unit of any other securities subject to then outstanding Options and Stock Appreciation Rights (without change in the aggregate purchase price as to which such Options or Rights remain exercisable), and (iv) the repurchase price of each share of Restricted Stock then subject to a Risk of Forfeiture in the form of a Company repurchase right.

8.2. **Adjustment of Awards Upon the Occurrence of Certain Unusual or Nonrecurring Events.** In the event of any corporate action not specifically covered by the preceding Section, including but not limited to an extraordinary cash distribution on Stock, a corporate separation or other reorganization or liquidation, the Committee shall make such adjustment of outstanding Awards and their terms, if any, as it, in its sole discretion, may deem equitable in the circumstances. The Committee may make adjustments in the terms and conditions of, and the criteria included in, Awards in recognition of unusual or nonrecurring events (including, without limitation, the events described in this Section) affecting the Company or the financial statements of the Company or of changes in applicable laws, regulations, or accounting principles, whenever the Committee determines that such adjustments are appropriate in order to prevent dilution or enlargement of the benefits or potential benefits intended to be made available under the Plan.

8.3. Related Matters. Any adjustment in Awards made pursuant to Section 8.1 or Section 8.2 shall be determined and made, if at all, by the Committee, acting in its sole discretion, and shall include any correlative modification of terms, including of Option exercise prices, rates of vesting or exercisability, Risks of Forfeiture, applicable repurchase prices for Restricted Stock, and Performance Goals and other business objectives which the Committee may deem necessary or appropriate so as to ensure the rights of the Participants in their respective Awards are not substantially diminished nor enlarged as a result of the adjustment and corporate action other than as expressly contemplated in this Section 8. The Committee, in its discretion, may determine that no fraction of a share of Stock shall be purchasable or deliverable upon exercise, and in that event if any adjustment hereunder of the number of shares of Stock covered by an Award would cause such number to include a fraction of a share of Stock, such number of shares of Stock shall be adjusted to the nearest smaller whole number of shares. No adjustment of an Option exercise price per share pursuant to Section 8.1 or Section 8.2 shall result in an exercise price which is less than the par value of the Stock.

8.4. Transactions.

(a) Definition of Transaction. In this Section 8.4, “Transaction” means (1) any merger or consolidation of the Company with or into another entity as a result of which the Stock of the Company is converted into or exchanged for the right to receive cash, securities or other property or is cancelled, (2) any sale or exchange of all or substantially all of the outstanding Stock of the Company for cash, securities or other property, (3) any sale, transfer, or other disposition of all or substantially all of the Company’s assets to one or more other persons in a single transaction or series of related transactions or (4) any liquidation or dissolution of the Company.

(b) Treatment of Awards. In a Transaction, the Committee may take any one or more of the following actions as to all or any (or any portion of) outstanding Awards, subject to the provisions of Section 9 of this Plan.

(1) Provide that any Awards shall be assumed, or substantially equivalent rights shall be provided in substitution therefor, by the acquiring or succeeding entity (or an affiliate thereof).

(2) Upon written notice to the holders, provide that all or any of the holders’ unexercised outstanding Options and Stock Appreciation Rights (collectively, “Rights”) will terminate immediately prior to the consummation of such Transaction unless exercised within a specified period following the date of such notice.

(3) Provide that all or any Awards that are subject to Risk of Forfeiture will terminate immediately prior to the consummation of such Transaction.

(4) Provide that all or any outstanding Rights shall Accelerate so as to become exercisable prior to or upon such Transaction with respect to some or all of the shares of Stock for which any such Rights would not then otherwise be exercisable by their terms.

(5) Provide that all or any outstanding Awards that are subject to Risk of Forfeiture shall Accelerate so that the Risk of Forfeiture otherwise applicable to such Awards shall expire prior to or upon such Transaction with respect to any such Awards that would then still otherwise be subject to the Risk of Forfeiture.

(6) Provide for cash payments, net of applicable tax withholdings,

to be made to holders equal to the excess, if any, of (A) the acquisition price times the number of shares of Stock subject to an Option and Stock Appreciation Right (in each case, to the extent the exercise price does not exceed the acquisition price) over (B) the aggregate exercise price for all such shares of Stock subject to the Option or Stock Appreciation Right as applicable, in exchange for the termination of such Option and Stock Appreciation Right; provided, that if the acquisition price does not exceed the exercise price of any such Option or Stock Appreciation Right, the Committee may cancel that Option and Stock Appreciation Right without the payment of any consideration therefore prior to or upon the Transaction. For purposes of this paragraph 6 and paragraph 7 below, “acquisition price” means the amount of cash, and market value of any other consideration, received in payment for a share of Stock surrendered in a Transaction but need not take into account any deferred consideration unless and until received.

(7) Provide for cash payments, net of applicable tax withholdings, to be made to holder or holders of all or any Awards (other than Options and Stock Appreciation Rights) equal to the acquisition price times the number of shares of Stock subject to any such Awards, in exchange for the termination of any such Awards; provided, that the Committee may cancel, pursuant to paragraph 3 above, any such Award that is subject to a Risk of Forfeiture at the time of the consummation of such Transaction without the payment of any consideration therefor prior to or upon the Transaction.

(8) Provide that, in connection with a liquidation or dissolution of the Company, all or any Awards (other than Restricted Stock or Stock Grants) shall convert into the right to receive liquidation proceeds net of the exercise price thereof and any applicable tax withholdings.

(9) Any combination of the foregoing.

In the event that the Committee determines in its discretion to take the actions contemplated under paragraph (1) above of this Section 8.4(b) with respect to all or any Awards, the Committee shall ensure that, upon consummation of the Transaction, any such Awards are assumed and/or exchanged or replaced with another similar award issued by the acquiring or succeeding entity (or an affiliate thereof) and that, as a result of such assumption and/or exchange or replacement, the holder of such assumed Award and/or such exchanged or replaced similar award has the right to purchase or receive the value of, for each share of Stock subject to such Award immediately prior to the consummation of the Transaction, the consideration (whether cash, securities or other property) received as a result of the Transaction by holders of Stock for each share of Stock held immediately prior to the consummation of the Transaction (and if holders were offered a choice of consideration, the type of consideration chosen by the holders of a majority of the outstanding shares of Stock); *provided, however*, that if such consideration received as a result of the Transaction is not solely common stock (or its equivalent) of the acquiring or succeeding entity (or an affiliate thereof), the Committee may, with the consent of the acquiring or succeeding entity (or an affiliate thereof), provide for the consideration to be

received with respect to such assumed Award and/or such exchanged or replaced similar award to consist of or be based solely on common stock (or its equivalent) of the acquiring or succeeding entity (or an affiliate thereof) equivalent in value to the per share consideration received by holders of outstanding shares of Stock as a result of the Transaction; and *provided, further*, that if such Award is an Option, the holder of such Option must exercise the Option and make payment of the applicable exercise price in connection therewith in order to receive such consideration.

(c) **Treatment of Other Awards.** Upon the occurrence of a Transaction other than a liquidation or dissolution of the Company which is not part of another form of Transaction, then, subject to the provisions of Section 9 below, with respect to all outstanding Awards (other than Options and Stock Appreciation Rights) that are not terminated prior to or upon such Transaction, the repurchase and other rights of the Company under each such Award shall inure to the benefit of the Company's successor and any forfeiture restrictions shall continue to apply and shall, unless the Committee determines otherwise, apply to the cash, securities or other property which the Stock was converted into or exchanged for pursuant to such Transaction in the same manner and to the same extent as they applied to the Award.

(d) **Related Matters.** In taking any of the actions permitted under this Section 8.4, the Committee shall not be obligated to treat all Awards, all Awards held by a Participant, or all Awards of the same type, identically. Any determinations required to carry out the foregoing provisions of this Section 8.4, including but not limited to the market value of other consideration received by holders of Stock in a Transaction and whether substantially equivalent Rights have been substituted, shall be made by the Committee acting in its sole discretion. In connection with any action or actions taken by the Committee in respect of Awards and in connection with a Transaction, the Committee may require such acknowledgements of satisfaction and releases from Participants as it may determine.

9. Change of Control

Except as otherwise provided below, upon the occurrence of a Change of Control, to the extent that the surviving entity declines to continue, convert, assume or replace outstanding Awards, then, notwithstanding anything express or implied to the contrary in Section 8.4 above:

(a) any and all Options and Stock Appreciation Rights not already exercisable in full shall Accelerate with respect to 100% of the shares for which such Options or Stock Appreciation Rights are not then exercisable;

(b) any Risk of Forfeiture applicable to Restricted Stock and Restricted Stock Units which is not based on achievement of Performance Goals or other business objectives shall lapse with respect to 100% of the Restricted Stock and Restricted Stock Units still subject to such Risk of Forfeiture immediately prior to the Change of Control; and

(c) all outstanding Awards of Restricted Stock and Restricted Stock Units conditioned on the achievement of Performance Goals or other business objectives and the payouts attainable under outstanding Performance Units shall be deemed to have been satisfied at target as of the effective date of the Change of Control, except if and to the extent otherwise determined by the Committee in its sole discretion at any time prior to, or upon, such Change of Control.

All such Awards of Performance Units and Restricted Stock Units shall be paid to the extent earned to Participants in accordance with their terms within thirty (30) days following the effective date of the Change of Control. None of the foregoing shall apply, however, (i) in the case of any Award pursuant to an Award Agreement requiring other or additional terms upon a Change of Control (or similar event), (ii) if specifically prohibited under applicable laws, or by the rules and regulations of any governing governmental agencies or national securities exchanges, or (iii) as otherwise provided in Section 7.7, concerning Qualified Performance-Based Awards.

10. Settlement of Awards

10.1. **In General.** Options and Restricted Stock shall be settled in accordance with their terms. All other Awards may be settled in cash, Stock, or other Awards, or a combination thereof, as determined

by the Committee at or after grant and subject to any contrary Award Agreement. The Committee may not require settlement of any Award in Stock pursuant to the immediately preceding sentence to the extent issuance of such Stock would be prohibited or unreasonably delayed by reason of any other provision of the Plan.

10.2. **Violation of Law.** Notwithstanding any other provision of the Plan or the relevant Award Agreement, if, at any time, in the reasonable opinion of the Company, the issuance of shares of Stock covered by an Award may constitute a violation of law, then the Company may delay such issuance until (i) approval shall have been obtained from such governmental agencies, other than the Securities and Exchange Commission, as may be required under any applicable law, rule, or regulation and (ii) in the case where such issuance would constitute a violation of a law administered by or a regulation of the Securities and Exchange Commission, one of the following conditions shall have been satisfied:

(a) the shares of Stock are at the time of the issue of such shares effectively registered under the Securities Act of 1933, as amended; or

(b) the Company shall have determined, on such basis as it deems appropriate (including an opinion of counsel in form and substance satisfactory to the Company) that the sale, transfer, assignment, pledge, encumbrance or other disposition of such shares does not require registration under the Securities Act of 1933, as amended or any applicable State securities laws.

Furthermore, the inability of the Company to obtain or maintain, or the impracticability of it obtaining or maintaining, authority from any governmental agency having jurisdiction, which authority is deemed by the Company's counsel to be necessary to the lawful issuance of any Stock hereunder, shall relieve the Company of any liability in respect of the failure to issue such Stock as to which such requisite authority shall not have been obtained, and shall constitute

circumstances in which the Committee may determine to amend or cancel Awards pertaining to such Stock, with or without consideration to the affected Participants.

10.3. Corporate Restrictions on Rights in Stock. Any Stock to be issued pursuant to Awards granted under the Plan shall be subject to all restrictions upon the transfer thereof which may be now or hereafter imposed by the certificate of incorporation, and bylaws.

10.4. Investment Representations. The Company shall be under no obligation to issue any shares of Stock covered by any Award unless the shares to be issued pursuant to Awards granted under the Plan have been effectively registered under the Securities Act of 1933, as amended, or the Participant shall have made such written representations to the Company (upon which the Company believes it may reasonably rely) as the Company may deem necessary or appropriate for purposes of confirming that the issuance of such shares will be exempt from the registration requirements of that Act and any applicable state securities laws and otherwise in compliance with all applicable laws, rules and regulations of any jurisdiction in which Participants may reside or primarily work, including but not limited to that the Participant is acquiring the shares for his or her own account for the purpose of investment and not with a view to, or for sale in connection with, the distribution of any such shares.

10.5. Registration. If the Company shall deem it necessary or desirable to register under the Securities Act of 1933, as amended, or other applicable statutes any shares of Stock issued or to be issued pursuant to Awards granted under the Plan, or to qualify any such shares of Stock for exemption from the Securities Act of 1933, as amended or other applicable statutes, then the Company shall take such action at its own expense. The Company may require from each recipient of an Award, or each holder of shares of Stock acquired pursuant to the Plan, such information in writing for use in any registration statement, prospectus, preliminary prospectus or offering circular as is reasonably necessary for that purpose and

may require reasonable indemnity to the Company and its officers and directors from that holder against all losses, claims, damage and liabilities arising from use of the information so furnished and caused by any untrue statement of any material fact therein or caused by the omission to state a material fact required to be stated therein or necessary to make the statements therein not misleading in the light of the circumstances under which they were made. In addition, the Company may require of any such person that he or she agree that, without the prior written consent of the Company or the managing underwriter in any public offering of shares of Stock, he or she will not sell, make any short sale of, loan, grant any option for the purchase of, pledge or otherwise encumber, or otherwise dispose of, any shares of Stock during the 180 day period commencing on the effective date of the registration statement relating to the underwritten public offering of securities (or during such shorter or longer period of time as the Committee shall determine in its sole discretion, which period of time shall commence from and after such effective date of such registration statement). Without limiting the generality of the foregoing provisions of this Section 10.5, if in connection with any underwritten public offering of securities of the Company the managing underwriter of such offering requires that the Company's directors and officers enter into a lock-up agreement containing provisions that are more restrictive than the provisions set forth in the preceding sentence, then (a) each holder of shares of Stock acquired pursuant to the Plan (regardless of whether such person has complied or complies with the provisions of clause (b) below) shall be bound by, and shall be deemed to have agreed to, the same lock-up terms as those to which the Company's directors and officers are required to adhere; and (b) at the request of the Company or such managing underwriter, each such person shall execute and deliver a lock-up agreement in form and substance equivalent to that which is required to be executed by the Company's directors and officers.

10.6. Placement of Legends; Stop Orders; etc. Each share of Stock to be issued pursuant to Awards granted under the Plan may bear a reference to the investment representations made in accordance with Section 10.4 in addition to any other applicable restrictions under the Plan, and the terms of the Award and, if applicable, to the fact that no registration statement has been filed with the Securities and Exchange Commission in respect to such shares of Stock. All shares of Stock or other securities issued under the Plan shall be subject to such stop transfer orders and other restrictions as the Committee may deem advisable under the rules, regulations, and other requirements of any stock exchange upon which the Stock is then listed, and any applicable federal or state securities law, and the Committee may cause a legend or legends to be placed on any such certificates to make appropriate reference to such restrictions, or, if the Stock will be held in book-entry position through the direct registration system of the Company's transfer agent, the restrictions will be appropriately noted.

10.7. Tax Withholding. Whenever shares of Stock are issued or to be issued pursuant to Awards granted under the Plan, the Company shall have the right to require the recipient to remit to the Company an amount sufficient to satisfy federal, state, local, foreign or other withholding tax requirements if, when, and to the extent required by law (whether so required to secure for the Company an otherwise available tax deduction or otherwise) prior to the delivery of any certificate or certificates, held in book-entry position through the direct registration system of the Company's transfer agent, for such shares. The obligations of the Company under the Plan shall be conditional on satisfaction of all such withholding obligations and the Company shall, to the extent permitted by law, have the right to deduct any such taxes from any payment of any kind otherwise due to a Participant or to utilize any other withholding method prescribed by the Committee from time to time. However, in such cases Participants may elect, subject to the approval of the Committee, acting in its sole discretion, to satisfy an applicable withholding requirement, in whole or in part, by having the Company withhold shares of Stock to satisfy their tax obligations. All elections shall be irrevocable, made in writing, signed by the Participant, and shall be subject to any restrictions or limitations that the Committee deems appropriate. If shares of Stock are withheld to satisfy an applicable withholding requirement, the shares of Stock withheld shall have a Market Value on the date the tax is to be determined equal to the minimum statutory total tax (or tax calculated at such higher rates as determined by the Committee) which could be imposed on the

transaction.

10.8. Company Certificate of Incorporation and Bylaws; Other Company Policies. This Plan and all Awards granted hereunder are subject to the certificate of incorporation and bylaws of the Company, as they may be amended from time to time, and all other Company policies duly adopted by the Board, the Committee or any other committee of the Board and as in effect from time to time regarding the acquisition, ownership or sale of Stock by officers, employees, directors, consultants, advisors and other service providers, including, without limitation, policies intended to limit the potential for insider trading and to avoid or recover compensation payable or paid on the basis of inaccurate financial results or statements, employee conduct, and other similar events.

11. **Reservation of Stock**

The Company shall at all times during the term of the Plan and any outstanding Awards granted hereunder reserve or otherwise keep available such number of shares of Stock as will be sufficient to satisfy the requirements of the Plan (if then in effect) and the Awards and shall pay all fees and expenses

necessarily incurred by the Company in connection therewith.

12. Limitation of Rights in Stock; No Special Service Rights

A Participant shall not be deemed for any purpose to be a stockholder of the Company with respect to any of the shares of Stock subject to an Award, unless and until a certificate shall have been issued therefor and delivered to the Participant or his agent, or the Stock shall be issued through the direct registration system of the Company's transfer agent. Any Stock to be issued pursuant to Awards granted under the Plan shall be subject to all restrictions upon the transfer thereof which may be now or hereafter imposed by the certificate of incorporation and the bylaws of the Company. Nothing contained in the Plan or in any Award Agreement shall confer upon any recipient of an Award any right with respect to the continuation of his or her employment or other association with the Company (or any Affiliate), or interfere in any way with the right of the Company (or any Affiliate), subject to the terms of any separate employment or consulting agreement or provision of law or certificate of incorporation or bylaws to the contrary, at any time to terminate such employment or consulting agreement or to increase or decrease, or otherwise adjust, the other terms and conditions of the recipient's employment or other association with the Company and its Affiliates.

13. Unfunded Status of Plan

The Plan is intended to constitute an "unfunded" plan for incentive compensation, and the Plan is not intended to constitute a plan subject to the provisions of the Employee Retirement Income Security Act of 1974, as amended. With respect to any payments not yet made to a Participant by the Company, nothing contained herein shall give any such Participant any rights that are greater than those of a general creditor of the Company. In its sole discretion, the Committee may authorize the creation of trusts or other arrangements to meet the obligations created under the Plan to deliver Stock or payments with respect to Awards hereunder, provided, however, that the existence of such trusts or other arrangements is consistent with the unfunded status of the Plan.

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14. Nonexclusivity of the Plan

Neither the adoption of the Plan by the Board nor any action taken in connection with the adoption or operation of the Plan shall be construed as creating any limitations on the power of the Board to adopt such other incentive arrangements as it may deem desirable, including without limitation, the granting of stock options and restricted stock other than under the Plan, and such arrangements may be either applicable generally or only in specific cases.

15. No Guarantee of Tax Consequences

It is intended that all Awards shall be granted and maintained on a basis which ensures they are exempt from, or otherwise compliant with, the requirements of Section 409A of the Code, pertaining non-qualified plans of deferred compensation, and the Plan shall be governed, interpreted and enforced consistent with such intent. However, neither the Company nor any Affiliate, nor any director, officer, agent, representative or employee of either, guarantees to the Participant or any other person any particular tax consequences as a result of the grant of, exercise of rights under, or payment in respect of an Award, including but not limited to that an Option granted as an Incentive Option has or will qualify as an "incentive stock option" within the meaning of Section 422 of the Code or that the provisions and penalties of Section 409A of the Code will or will not apply and no person shall have any liability to a Participant or any other party if a payment under an Award that is intended to benefit from favorable tax treatment or avoid adverse tax treatment fails to realize such intention or for any action taken by the Board or the Committee with respect to the Award.

16. Termination and Amendment of the Plan

16.1. Termination or Amendment of the Plan. Subject to the limitations contained in Section 16.3 below, including specifically the requirement of stockholder approval, if applicable, the Committee may at any time suspend or terminate the Plan or make such modifications of the Plan as it shall deem advisable. Unless the Committee otherwise expressly provides, no amendment of the Plan shall affect the terms of any Award outstanding on the date of such amendment.

16.2. Termination or Amendment of Outstanding Awards; Assumptions. Subject to the limitations contained in Section 16.3 below, including specifically the requirement of stockholder approval, if applicable, the Committee may at any time:

- (a) amend the terms of any Award theretofore granted, prospectively or retroactively, provided that the Award as amended is consistent with the terms of the Plan;
- (b) within the limitations of the Plan, modify, extend or assume outstanding Awards or accept the cancellation of outstanding Awards or of outstanding stock options or other equity-based compensation awards granted by another issuer in return for the grant of new Awards for the same or a different number of shares of Stock and on the same or different terms and conditions (including but not limited to the exercise price of any Option); and
- (c) offer to buy out for a payment in cash or cash equivalents an Award previously granted or authorize the recipient of an Award to elect to cash out an Award previously granted, in either case at such time and based upon such terms and conditions as the Committee shall establish.

16.3. Limitations on Amendments, Etc.

(a) Without the approval of the Company's stockholders, no amendment or modification of the Plan by the Committee may (i) increase the number of shares of Stock which may be issued under the Plan, (ii) change the description of the persons eligible for Awards, or (iii) effect any

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other change for which stockholder approval is required by law or the rules of any relevant stock exchange. Awards may be made under the Plan that involve shares of Stock in excess of the number of shares then available for issuance under the Plan, provided no shares shall actually be issued pursuant to those Awards until the number of shares of Stock available for issuance under the Plan is sufficiently increased by stockholder approval of an amendment of the

Plan authorizing such increase. If such stockholder approval is not obtained within twelve (12) months after the date the first excess Award is made, then all Awards granted on the basis of such excess shares shall terminate and cease to be outstanding.

(b) No action by the Board or the Committee pursuant to this Section 16 shall impair the rights of the recipient of any Award outstanding on the date of such amendment or modification of such Award, as the case may be, without the Participant's consent; *provided, however,* that no such consent shall be required (A) in the case of any amendment or termination of any outstanding Award that is permitted by any provision of this Plan that is set forth in Section 8, Section 9 or in any other section of this Plan that is not Section 16.2 or (B) if the Board or Committee, as the case may be, (i) determines in its sole discretion and prior to the date of any Change of Control that such amendment or alteration either is required or advisable in order for the Company, the Plan or the Award to satisfy any law or regulation, including without limitation the provisions of Section 409A of the Code, or to meet the requirements of or avoid adverse financial accounting consequences under any accounting standard, (ii) determines in its sole discretion and prior to the date of any Change of Control that such amendment or alteration is not reasonably likely to significantly diminish the benefits provided under the Award, or that any such diminution has been adequately compensated, or (iii) reasonably determines on or after the date of Change of Control that such amendment or alteration either is required or advisable in order for the Company, the Plan or the Award to satisfy any law or regulation, including without limitation the provisions of Section 409A of the Code.

17. Recoupment

Participants shall be subject to any clawback, recoupment or other similar policy adopted by the Board as in effect from time to time and Awards and any cash, shares of Stock or other property or amounts due, paid or issued to a Participant shall be subject to the terms of such policy, as in effect from time to time.

18. Notices and Other Communications

Any communication or notice required or permitted to be given under the Plan shall be in such form as the Committee may determine from time to time. If a notice, demand, request or other communication is required or permitted to be given in writing, then any such notice, demand, request or other communication hereunder to any party shall be deemed to be sufficient if contained in a written instrument delivered in person or duly sent by first class registered, certified or overnight mail, postage prepaid, or by facsimile with a confirmation copy by regular, certified or overnight mail, addressed or by facsimile, as the case may be, (i) if to the recipient of an Award, at his or her residence address last filed with the Company and (ii) if to the Company, at its principal place of business, addressed to the attention of its Treasurer, or to such other address or facsimile number, as the case may be, as the addressee may have designated by notice to the addressor. All such notices, requests, demands and other communications shall be deemed to have been received: (i) in the case of personal delivery, on the date of such delivery; (ii) in the case of mailing, when received by the addressee; and (iii) in the case of facsimile transmission, when confirmed by facsimile machine report.

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19. Governing Law

The Plan and all Award Agreements and actions taken hereunder and thereunder shall be governed, interpreted and enforced in accordance with the laws of the State of Delaware, without regard to the conflict of laws principles thereof.

[End of document.]

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RHYTHM PHARMACEUTICALS, INC. 2017 EQUITY INCENTIVE PLAN

STOCK OPTION AGREEMENT

THIS STOCK OPTION AGREEMENT, dated as of [] , 20] (this “Agreement”), is between Rhythm Pharmaceuticals, Inc., a corporation organized under the laws of the State of Delaware (the “Company”), and the individual identified in paragraph 1 below, currently residing at the address set out at the end of this Agreement (the “Optionee”). Capitalized terms used in this Agreement without definition shall have the respective meaning ascribed to such capitalized terms in the Plan (as defined below).

1. Grant of Option. Pursuant and subject to the Company’s 2017 Equity Incentive Plan (as the same may be amended from time to time, the “Plan”), the Company grants to you, the Optionee identified in the table below, an option (the “Option”) to purchase from the Company all or any part of a total of the number of shares identified in the table below (the “Optioned Shares”) of the common stock, par value \$0.001 per share, in the Company (the “Stock”), at the exercise price per share set out in the table below.

Optionee

Number of Shares

Exercise Price Per Share

Grant Date

Expiration Date(2)

2. Character of Option. This Option [is/is not](3) intended to be treated as an “incentive stock option” within the meaning of Section 422 of the Internal Revenue Code of 1986, as amended.

3. Expiration of Option. This Option shall expire at 5:00 p.m. EST on the Expiration Date or, if earlier, the earliest of the dates specified in whichever of the following applies:

- a) If the termination of your employment or other association is on account of your death or disability, the first anniversary of the date your employment ends.
- b) If the termination of your employment or other association is due to any other reason, three (3) months after your employment or other association ends.

(2) For ISOs, not later than the day immediately preceding the tenth anniversary of the Grant Date.

(3) Either "is" or "is not", as the Committee or the Board has determined.

4. Exercise of Option.

a) You may exercise this Option, in full or in part and at any time prior to the date this Option expires, as to the number of Optioned Shares for which this Option shall have become exercisable (the "Vested Shares") pursuant Section 4(b) below. However, during any period that this Option remains outstanding after the end of your association with the Company and its Affiliates in any and all capacities as an officer, director, employee and/or consultant of the Company and its Affiliates, you may exercise it only to the extent of any remaining Vested Shares determined as of the effective time of the end of such association. The procedure for exercising this Option is described in Section 7.1(f) of the Plan; provided that in no event shall a fraction of a share of Stock be purchasable or deliverable upon exercise.

b) [Vesting terms to be inserted]

c)

Number of Shares in Each Installment	Initial Exercise Date for Shares in Installment

5. Transfer of Option. You may not transfer this Option except by will or the laws of descent and distribution, and, during your lifetime, only you may exercise this Option.

6. Incorporation of Plan Terms. This Option is granted subject to all of the applicable terms and provisions of the Plan, including but not limited to the limitations on the Company's obligation to deliver Optioned Shares upon exercise set forth in Section 9 therein.

7. Tax Consequences. The Company makes no representation or warranty as to the tax treatment to you of your receipt or exercise of this Option or upon your sale or other disposition of the Optioned Shares. You should rely on your own tax advisors for such advice.

8. Treatment as Wages or Compensation. No amounts paid or payable in connection with this Option shall constitute wages or compensation for purposes of any applicable law, if ever, prior to the date on which such amount has been earned, vested and become payable in accordance with the terms of this Agreement and the Plan. No such amount shall be treated as wages or compensation for purposes of any employee or other benefit plan of the Company and its Affiliates except to the extent and at the time provided in the respective employee or other benefit plan.

9. Acknowledgements. You acknowledge that you have reviewed and understand the Plan and this Agreement in their entirety, and have had an opportunity to obtain the advice of counsel prior to executing this Agreement. You hereby agree to accept as binding, conclusive and final all decisions or interpretations of the Committee upon any questions arising under the Plan or this Agreement.

10. Further Assurances. The parties agree to execute such further instruments and to take such action as may reasonably be necessary to carry out the intent of this Agreement.

[11. Community Property.] Without prejudice to the actual rights of the spouses as between each other, for all purposes of this Agreement, you shall be treated as agent and attorney-in-fact for that interest held or claimed by your spouse with respect to this Option and any Optioned Shares and the parties hereto shall act in all matters as if the Optionee was the sole owner of this Option and (following exercise) any such Optioned Shares. This appointment is coupled with an interest and is irrevocable.](4)

12. Miscellaneous. This Agreement shall be construed and enforced in accordance with the laws of the State of Delaware, without regard to the conflict of laws principles thereof and shall be binding upon and inure to the benefit of any successor or assign of the Company and any executor, administrator, trustee, guardian, or other legal representative of you. Capitalized terms used but not defined herein shall have the meaning assigned under the Plan. This Agreement may be executed in one or more counterparts all of which together shall constitute but one instrument. In making proof of this Agreement it shall not be necessary to produce or account for more than one such counterpart.

RHYTHM PHARMACEUTICALS, INC.
2017 EQUITY INCENTIVE PLAN

OPTION EXERCISE FORM

Rhythm Pharmaceuticals, Inc.
500 Boylston Street, 11th Floor
Boston, MA 02116

Attention: Controller

Dear Sir:

In accordance with, and subject to the terms and conditions of, the Rhythm Pharmaceuticals, Inc. 2017 Equity Incentive Plan, as amended and in effect to date, I hereby elect to exercise my option granted under the agreement dated _____, to purchase _____ shares of the common stock, par value \$0.001 per share, in Rhythm Pharmaceuticals, Inc. (the "Company").

Enclosed herewith is payment to the Company in the amount of \$ _____ in full payment of the option price of \$ _____ per share, for said shares. [To be revised as necessary for non-cash payment of exercise price.]

Sincerely yours,

Name:

RHYTHM PHARMACEUTICALS, INC. REQUESTS THAT THE MARKED
PORTIONS OF THIS EXHIBIT BE GRANTED CONFIDENTIAL TREATMENT
UNDER RULE 406 OF THE SECURITIES ACT OF 1933, AS AMENDED

EXECUTION VERSION

LICENSE AGREEMENT
BY AND BETWEEN
CAMURUS AB
AND
RHYTHM PHARMACEUTICALS, INC.

CONFIDENTIAL

* CONFIDENTIAL TREATMENT REQUESTED. OMITTED PORTIONS FILED WITH THE SECURITIES AND EXCHANGE COMMISSION
PURSUANT TO RULE 406 PROMULGATED UNDER THE SECURITIES ACT OF 1933, AS AMENDED

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LICENSE AGREEMENT

This License Agreement is made as off the Effective Date (hereinafter defined) between **Camurus AB**, a limited liability company organized and existing under the laws of Sweden and having its principal place of business at Ideon Science Park, Sölvegatan 41, SE-223 70 Lund, Sweden (“**Camurus**”) and **Rhythm Pharmaceuticals, Inc.**, a corporation organized and existing under the laws of Delaware and having its principal place of business at 855 Boylston Street, 11th Floor, Boston, MA 02116 USA (“**Rhythm**”) (each a “**Party**” and collectively, the “**Parties**”)

WITNESSETH

WHEREAS, Camurus is the owner of all right, title and interest in and to certain patents and know-how relating to the FC Technology (as defined below) which delivers therapeutic levels of drug substance over extended periods by offering a lipid based injectable liquid solution that, within minutes after

injection, forms a controlled release liquid crystal gel matrix in situ on contact with body fluids at site of injection;

WHEREAS, Rhythm has capabilities in the development, manufacture, promotion, marketing, sales and life cycle management of pharmaceutical products and is the owner of all right, title and interest in and to a drug compound known as RM-493;

WHEREAS, Rhythm wishes to obtain an exclusive world-wide license to the FC technology to formulate RM-493 and to develop, manufacture, promote, market, distribute and sell the Product (as defined below) in the Territory (as defined below); and

WHEREAS, Camurus is willing to grant such world-wide exclusive rights to Rhythm in respect of the Product upon the terms and conditions hereinafter set forth.

NOW, THEREFORE, in consideration of the covenants and obligations expressed herein, and intending to be legally bound, the Parties agree as follows:

1 DEFINITIONS

- 1.1 **"Adverse Events"** has the meaning ascribed to it in Section 3.8.
- 1.2 **"Affiliate"** means, with respect to a Party, any entity or person that controls, is controlled by, or is under common control with that Party. For the purpose of this definition, "control" or "controlled" means, direct or indirect, ownership of fifty percent (50%) or more of the shares of stock entitled to vote for the election of directors in the case of a corporation or fifty percent (50%) or more of the equity interest in the case of any other type of legal entity; status as a general partner in any partnership; or any other arrangement whereby the entity or person controls or has the right to control the board of directors or equivalent governing body of a corporation or other entity or the ability to cause the direction of the management or policies of a corporation or other entity. The Parties acknowledge that in the case of entities organized under the laws of certain countries where the maximum percentage ownership permitted by law for a foreign investor is less than fifty

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percent (50%), such lower percentage shall be substituted in the preceding sentence, provided that such foreign investor has the power to direct the management and policies of such entity.

- 1.3 **"Business Day"** means Monday through Friday, other than holidays observed by Camurus or Rhythm.
- 1.4 **"Camurus IP"** means (a) the Camurus Platform IP and (b) Camurus' interest in any Joint IP.
- 1.5 **"Camurus Platform IP"** means (a) all Patent Rights listed in Exhibit 1.5 and (b) all other Intellectual Property Controlled by Camurus or any of its Affiliates during the Term hereof that covers the FC Technology.
- 1.6 **"Camurus Platform Patents"** has the meaning ascribed to it in Section 7.3.
- 1.7 **"Camurus Trademark"** means Trademarks Controlled by Camurus, including FluidCrystal® and other Trademarks described in Exhibit 1.7, that relate to the FC Technology.
- 1.8 **"GCP"** means Good Clinical Practices, as set forth in the ICH Harmonized Guidance on Good Clinical Practice (CPMP/ICH/135/95).
- 1.9 **"GMP"** means Good Manufacturing Practices, as set forth in the Rules Governing Medicinal Product in the European Union volume 4 and the equivalent requirements and/or applicable guidance in any other jurisdiction in the Territory.
- 1.10 **"Clinical Trials"** means human clinical trials conducted on healthy volunteers or patients to provide data supporting Regulatory Approval of such drug or label expansion of such drug,
- 1.11 **"CMO"** means one or more Third Party contract manufacturing organization(s) that may be used to source ingredients, components, packaging materials and the like and to manufacture, package, label and quality release Rhythm's requirements for Product for use and/or sale in the Territory, all pursuant to the Rhythm Supply Agreement.
- 1.12 **"Collaboration Inventions"** means all Intellectual Property conceived and reduced to practice by a Party or any of its Affiliates or by a Third Party on behalf of such Party in the course of performing activities under this Agreement or any of Rhythm's licensees or Sub-licensees.
- 1.13 **"Collaboration Product Patents"** has the meaning ascribed to it in Section 7.3(b) hereof.
- 1.14 **"Commercially Reasonable Efforts"** means the level of effort and resources required to develop the Product in a sustained manner consistent with the efforts an international specialty pharmaceutical company of similar size and resources would typically devote to a product owned by such entity which is of similar market potential, at a similar stage in the development or life of such product, taking into account issues of safety, efficacy, product profile, the competitiveness of the

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marketplace, the proprietary position of the product, the regulatory structure involved, profitability of the product and other relevant commercial factors.

- 1.15 **“Competing Product”** means any pharmaceutical product comprising []*.
- 1.16 **“Confidential Information”** means the following, subject to the exceptions set forth in Section 8.1:
- (i) the terms and conditions of this Agreement, for which each Party will be considered a Disclosing Party and a Recipient;
 - (ii) Know-How within Camurus IP for which Camurus will be considered the Disclosing Party and Rhythm shall be the Recipient;
 - (iii) Know-How within Rhythm IP for which Rhythm will be considered the Disclosing Party and Camurus shall be the Recipient; and
 - (iv) any other non-public information, whether or not patentable, disclosed or provided by one Party to the other Party in connection with this Agreement, including, without limitation, information regarding such Party’s strategy, business plans, objectives, research, technology, products, IP strategy, business affairs or finances including information of the type that is customarily considered to be confidential information by parties engaged in activities that are substantially similar to the activities being engaged in by the Parties under this Agreement, for which the Party making such disclosure will be considered the Disclosing Party and the receiver will be the Recipient.
- 1.17 **“Control” or “Controlled”** means possession by a Party of the right to grant to the other Party a license, sublicense or other right to use, of the scope provided for in this Agreement, to Intellectual Property and rights to access or cross-reference regulatory filings without violating the terms of any agreement or other arrangement with any Third Party.
- 1.18 **“Development Data”** means all chemistry, manufacturing and control, preclinical and clinical data including, without limitation, pharmacological, pharmacokinetic, pharmaceutical development and toxicological data, on the Product (including placebo), including any of the foregoing arising from post registration studies, that is generated at any time during the Term of this Agreement by or for either Party and their Affiliates or any of Rhythm’s licensees or sub-licensees.
- 1.19 **“Development Plan”** means Rhythm’s plan for pre-clinical and clinical development of the Product together with associated budget through the Ph1B PK/POC Study. The Development Plan as in effect as of the Effective Date is attached hereto as Exhibit 1.19. The Development Plan is subject to update in accordance with Section 3.1 hereof.
- 1.20 **“Disclosing Party”** means the Party which discloses Confidential Information to the other Party.
- 1.21 **“Drug”** means Setmelanotide (also known as RM-493) with the chemical structure described in Exhibit 1.19, and its salts.

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- 1.22 **“Effective Date”** means the date of the signature of the last Party to execute this Agreement.
- 1.23 **“EMA”** means the European Medicines Agency and/or the Committee for Human Medicinal Product or any successor agency thereof or, to the extent the mutual recognition or decentralized procedure is used for a Product in the EU, any national governmental authority having the authority to regulate the sale of medicinal pharmaceutical products in any country in the EU.
- 1.24 **“FC Technology”** means (i) Camurus’ proprietary formulation technology that is referred to as FluidCrystal® injection depot technology, comprising a lipid based injectable liquid solution that, within minutes after injection, forms a controlled release liquid crystal gel matrix in situ on contact with body fluids at the site of injection, including modifications and improvements to such proprietary formulation technology, and (ii) any other controlled release lipid formulation for injection that is conceived and reduced to practice by, or on behalf of, Camurus and that incorporates any active pharmaceutical ingredient without relating specifically to the Drug, Product or Competing Product excluding for the avoidance of doubt controlled release lipid formulations for injection that are developed by a Third Party and acquired by Camurus through licensing, acquisition, merger or otherwise..
- 1.25 **“First Commercial Sale”** means the date on which a Product is first sold following Regulatory Approval in the Territory by Rhythm or any of its Affiliates or Sublicensees to a Third Party (other than sales by Rhythm to its Affiliates or Sublicensees) in a commercial arm’s length transaction.
- 1.26 **“First Product Patent Application”** means a patent application filed by Rhythm with the United States Patent and Trademark Office pursuant to Section 7.3(d) hereof that specifically claims the Product.
- 1.27 **“FTE”** means a full time equivalent person year equal to at least 1,650 hours per year of work carried out by an employee.
- 1.28 **“FTE Costs”** means the cost of FTEs at the FTE Rate.
- 1.29 **“FTE Rate”** means the price of a single FTE per Calendar Year. The FTE Rate shall be US\$[]* per hour for all staff. The FTE Rate reflects the fully burdened internal costs of an FTE including all employee-related compensation, including but not limited to, salaries, wages, bonuses, benefits, profit sharing, share option grants, and any other employment costs, including travel and associated subsistence costs (but excluding travel and subsistence costs incurred in any travel) and professional dues and allocable overhead. On the 1 January each Calendar Year, commencing with 1 January 2016, the FTE Rate will be increased by the percentage (%) increase in inflation as measured by the Swedish Consumer Price Index

1.30 **“GAAP”** means U.S. Generally Accepted Accounting Principles, consistently applied.

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1.31 **“Generic Product”** means a product approved under an Abbreviated New Drug Application, or ANDA, or any non-United States equivalent filing, with the Product as the reference product, that is “therapeutically equivalent” as evidenced by the assignment of any ‘A’ level therapeutic equivalence rating by the FDA, or any non-United States equivalent rating, such that the product is therapeutically equivalent to the Product, or otherwise is generally substitutable by the pharmacist for the Product when filling a prescription written for the Product without having to seek authorization to do so from the physician writing such prescription.

1.32 **“IND”** means an Investigational New Drug application (together with all subsequent submissions, supplements and amendments thereto, and any materials, documents or information referred to or relied upon thereby) filed with the FDA in conformance with applicable laws and regulations, and the equivalent thereof (or other right to commence clinical testing in humans), as applicable, in jurisdictions outside the United States.

1.33 **“Intellectual Property” or “IP”** means any Patent Rights, Trademarks, Know-How, Confidential Information, and any other intellectual property rights.

1.34 **“Joint Invention”** shall have the meaning defined in Section 7.2(c).

1.35 **“Joint IP”** means any Joint Invention and any Patent Rights claiming any Joint Invention.

1.36 **“Joint Patents”** has the meaning ascribed to it in Section 7.3 (c).

1.37 **“JDC”** means the Joint Development Committee referred to in Section 3.3.

1.38 **“Know-How”** means technical and other information which is not in the public domain, including information comprising or relating to concepts, trade secrets, data, designs, discoveries, formulae, ideas, inventions, materials, methods, models, research plans, procedures, designs for experiments and tests and results of experimentation and testing (including results of research or development), processes (including manufacturing processes, specifications and techniques), laboratory records, chemical, pharmacological, toxicological, clinical, analytical and quality control data, clinical and non-clinical trial data, case report forms, data analyses, reports, manufacturing data or summaries and information contained in submissions to and information from ethical committees and regulatory authorities. Know-How includes documents containing Know-How, including any rights including trade secrets, copyright, database or design rights protecting such Know-How. The fact that an item is known to the public shall not be taken to preclude the possibility that a compilation including the item, and/or a development relating to the item, is not known to the public.

1.39 **“LIBOR”** has the meaning ascribed to it in Section 5.8.

1.40 **“Licensed Field”** means any and all uses including, but not limited to, the treatment, prevention or diagnosis of any disease, disorder or condition.

1.41 **“Manufacturing Costs”** means all []*.

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1.42 **“NDA”** means a new drug, biologic or other application, health registration, marketing authorization application, common technical document, regulatory submission, notice of compliance or equivalent application to the FDA or other applicable Regulatory Authority (excluding local and general business licenses and permits) required to be approved before commercial sale or use of the Product as a pharmaceutical or medicinal product in any formulation or dosage form (excluding any pricing and reimbursement approvals), together with all subsequent submissions, supplements and amendments thereto.

1.43 **“NDA Approval”** means approval of an NDA by the FDA or other applicable Regulatory Authority.

1.44 **“Net Sales”** means, with respect to any Product, the gross amount invoiced by Rhythm, its Affiliates or Sublicensees to unrelated Third Party distributors or agents (in each case, who are not sublicensees), or end users in the Territory for the sale or transfer for value of the applicable Product, less deductions for: (i) trade, quantity and cash discounts and rebates actually given to and taken by customers; (ii) refunds, chargebacks and any other allowances actually paid to or taken by customers, including those granted to managed care entities; (iii) amounts separately and actually credited to customers for Product returns, credits or allowances; (iv) rebates actually paid or credited to any governmental agency (or branch thereof) or to any Third Party payor, administrator or contractee (such as those in respect of any state or federal Medicare, Medicaid or similar programs); (v) discounts mandated by, or granted to meet the requirements of, applicable state, provincial or federal law, paid or credited to a wholesaler, purchaser, Third Party or other contractee including required chargebacks and retroactive price reductions; (vi) special outbound packing, freight, shipping insurance and other transportation expenses that are separately billed to the customer or prepaid; (vii) sales, value-added,

excise and turnover taxes, tariffs and duties, and other taxes directly related to the sale of the Product (but excluding net income taxes); and (viii) the actual amount of any write-offs for bad debt relating to such sales, provided when paid the amount shall be added to the Net Sales.

The amounts of any deductions taken pursuant to clauses (i)-(viii) shall be determined from books and records maintained in accordance with GAAP. This definition of Net Sales shall be updated as needed from time to time as appropriate to reflect changes required by (i) the adoption by Rhythm, as part of its ordinary business practices, consistently applied, of accounting standards other than GAAP or as required by law, or (ii) GAAP so long as Rhythm is utilizing GAAP as its accounting standard. Net Sales shall not include revenue received by Rhythm or any of its Affiliates from transactions with an Affiliate, where the Product in question will be resold to an independent third-party distributor or agent (in each case, who is not a Sublicensee) or end user by the Affiliate where such revenue received by the Affiliate from such resale is included in Net Sales. Revenue received by Rhythm (or any of its Affiliates) from transactions with an Affiliate, where the Product in question is used by the Affiliate solely for such Affiliate's internal purposes shall also be included in Net Sales at a price equal to the fair market value of such transfer(s).

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If the Product is sold in a bundled manner with other products or services of Rhythm then all such deductions shall be fairly and equitably allocated to the Product and other products or services of Rhythm, its Affiliates and Sublicensees, such that the Product does not bear a disproportionate portion of such deductions. The transfer of Product by Rhythm to an Affiliate or Sublicensee shall not be deemed a sale. Net Sales shall be calculated in accordance with generally accepted accounting principles in the United States (US GAAP), consistently applied.

1.45 **"Patent Right"** means (a) all national, regional and international patents and patent applications, including provisional patent applications; (b) all patent applications filed either from such patents, patent applications or provisional applications or from an application claiming priority from any of these, including utility applications, divisionals, continuations, continuations-in-part, provisionals, converted provisionals, and continued prosecution applications, and reissue applications; (c) any and all patents that have issued or in the future issue from the foregoing patent applications described in clauses (a) and (b), including author certificates, inventor certificates, utility models, petty patents and design patents and certificates of invention; (d) any and all extensions or restorations by existing or future extension or restoration mechanisms, including revalidations, reissues, re-examinations and extensions (including any supplementary protection certificates and the like) of the foregoing patents or patent applications described in clauses (a), (b) and (c); and (e) any similar rights, including so-called pipeline protection (where the subject matter previously disclosed was not previously patentable in a particular jurisdiction but subsequently becomes patentable subject matter in such jurisdiction), or any importation, revalidation, confirmation or introduction patent or registration patent or patent of additions to any such foregoing patent applications and patents.

1.46 **"Payment Report"** has the meaning ascribed to it in Section 5.7.

1.47 **"Ph1B PK/POC Study"** has the meaning ascribed to it in Section 3.6.

1.48 **"Product(s)"** means the Drug as sole active pharmaceutical ingredient formulated with the FC Technology for injection. For clarity, Products comprised of the same active pharmaceutical ingredient and delivered by similar drug administration methods (e.g., injection, such as by pen, syringe and needle, or needle-free) for same or different duration, or different doses of the same or different formulations of the FC Technology, shall be considered the same Product.

1.49 **"Prosecute" or "Prosecuting"** means with regard to specified Patent Rights, preparing, filing, prosecuting, validating, maintaining and defending such Patent Rights, including with respect to any re-examination, reissue, revocation, interference or opposition proceedings including any appeal therefrom. For the avoidance of doubt, "**Prosecuting**" excludes any infringement suits or other legal proceedings to enforce the specified Patent Rights, regardless of whether or not such proceedings involve the defense of the Patent Rights in suit.

1.50 **"Recipient"** means the Party, which receives Confidential Information from the other Party.

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1.51 **"Regulatory Approvals"** means any NDA Approvals and other approvals, licenses, registrations, or authorizations granted or issued by any Regulatory Authority necessary for the manufacture, packaging, labeling, use, storage, transport, export, import, clinical testing, promotion or sale of the Product in a country, including pricing and reimbursement approvals to the extent the applicable Regulatory Authority in such country require a pricing or reimbursement approval prior to commercialization of a Product in such country.

1.52 **"Regulatory Authority"** means any national, supranational, regional, state or local regulatory agency, department, bureau, commission, council or other governmental entity, including the FDA, in any country involved in the granting or receipt as the case may be of INDs, NDAs or Regulatory Approvals.

1.53 **"Rhythm Collaboration IP"** means all Collaboration Inventions owned by Rhythm pursuant to Section 7.2, 7.3 (d) or Section 7.4, including Rhythm's interest in any Joint IP.

1.54 **"Rhythm IP"** means the Rhythm Collaboration IP and the Rhythm Product IP.

- 1.55 **"Rhythm Product IP"** means (a) all Patent Rights; (b) all Know-How and all other Intellectual Property; in each of (a) and (b) that (1) are Controlled by Rhythm or any of its Affiliates as of the Effective Date or become Controlled by Rhythm or its Affiliates during the term hereof and (2) are necessary or useful to make or have made, use, offer to sell, sell, have sold, import, or otherwise exploit the Product. Notwithstanding the foregoing, Rhythm Product IP shall not include any Rhythm Collaboration IP.
- 1.56 **"Rhythm Product Patents"** means all Patent Rights within Rhythm Product IP.
- 1.57 **"Rhythm Supply Agreement"** means supply agreement between Rhythm and CMO governing the supply of the Product to Rhythm by CMO for the Territory.
- 1.58 **"Rhythm Trademarks"** means any Trademark owned or registered by Rhythm or that may be granted to Rhythm in the Territory to be used on the Product in the Territory and excluding any Camurus Trademarks.
- 1.59 **"Royalty Term"** has the meaning ascribed to it in Section 5.3.
- 1.60 **"Sublicensee"** shall have the meaning defined in Section 2.3.
- 1.61 **"Term"** shall have the meaning defined in Section 11.1.
- 1.62 **"Territory"** means the entire world.
- 1.63 **"Third Party"** means any entity other than Camurus or Rhythm or their respective Affiliates.
- 1.64 **"Trademarks"** means registered trademarks and applications therefor, unregistered trade or service marks and company names in each case with any and all associated

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- goodwill and all rights or forms of protection of a similar or analogous nature including rights which protect goodwill whether arising or granted under the laws of any jurisdiction and, for purposes of this definition, trade dress.
- 1.65 **"Valid Claim"** means a claim of a (i) granted patent which has not been revoked or held unenforceable or invalid by a decision of a court or other governmental agency of competent jurisdiction, which is not appealable or has not been appealed within the time allowed for appeal, and which has not been abandoned, disclaimed or surrendered, or (ii) an unissued published patent application that has not been formally terminated, abandoned, denied or admitted to be invalid or unenforceable through reissue, re-examination or disclaimer and which claim has been pending no longer than the earlier of (a) the date that is ten (10) years after the earliest priority date of the earliest application in which the claim could have been presented or (b) the date that is ten (10) years after the Effective Date, wherein after such earlier date such claim is expired and not a Valid Claim until the date that such a claim is granted or accepted for grant; provided, however, that if the holding of such court or agency with respect to a patent application is later reversed by a court or agency with overriding authority, the claim shall be reinstated as a Valid Claim with respect to Net Sales made after the date of such reversal.
- 1.66 Interpretation.
- Whenever any provision of this Agreement uses the term "including" (or "includes"), such term shall be deemed to mean "including without limitation" and "including but not limited to" (or "includes without limitations" and "includes but is not limited to") regardless of whether the words "without limitation" or "but not limited to" actually follow the term "including" (or "includes");
 - "Herein", "hereby", "hereunder", "hereof" and other equivalent words shall refer to this Agreement in its entirety and not solely to the particular portion of this Agreement in which any such word I used;
 - All definitions set forth herein shall be deemed applicable whether the words defined are used herein in the singular or the plural;
 - Wherever used herein, any pronoun or pronouns shall be deemed to include both the singular and plural and to cover all genders;
 - The recitals set forth at the start of this Agreement, along with the Exhibits to this Agreement, and the terms and conditions incorporated in such recital, Exhibits shall be deemed integral parts of this Agreement and all references in this Agreement to this Agreement shall encompass such recitals, Exhibits and the terms and conditions incorporated in such recitals, Exhibits, *provided*, that in the event of any conflict between the terms and conditions of this Agreement and any terms and conditions set forth in the Exhibits the terms of this Agreement shall control;
 - In the event of any conflict between the terms and conditions of this Agreement and any terms and conditions that may be set forth on any order, invoice, verbal agreement or otherwise, the terms and conditions of this Agreement shall govern;

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- The Agreement shall be construed as if both Parties drafted it jointly, and shall not be construed against either Party as principal drafter;

- Unless otherwise provided, all references to Sections and Exhibits in this Agreement are to Sections and Exhibits of and to this Agreement;
- Unless otherwise provided, all references to days, months, quarters or years are references to calendar days, calendar months, calendar quarters or calendar years;
- Any reference to any federal, national, state, local or foreign statute or law shall be deemed to also refer to all rules and regulations promulgated thereunder, unless to context requires otherwise; and
- Wherever used, the word “shall” and the word “will” are each understood to be imperative or mandatory in nature and are interchangeable with one another.

2 LICENSE GRANT TO RHYTHM

2.1 **License Grant.** Camurus hereby grants to Rhythm, and Rhythm hereby accepts, the exclusive royalty bearing license under the Camurus IP to develop, make or have made, use, sell, offer for sale, market and promote the Product in the Licensed Field in the Territory. The exclusive rights of Rhythm granted herein are subject to the rights required for Camurus to perform its obligations and exercise its rights under this Agreement.

2.2 **Subcontracting.** Subject to the terms of Section 2.3, Rhythm and its Affiliates shall have the right, without obtaining the written consent of Camurus, (i) to subcontract its development and manufacturing responsibilities under this Agreement (and grant any necessary sublicenses in connection therewith), and (ii) to engage contract sales organizations to supplement or complement Rhythm’s own sales force. Rhythm shall at all times be liable for all such activities as if such activities had been undertaken by Rhythm hereunder.

2.3 **Sublicenses.** Subject to Section 2.2 Rhythm may not grant sublicenses under the licenses granted under Section 2.1, except as follows.

- Rhythm may grant sublicenses to Camurus IP as required to make and have made the Product;
- Rhythm may grant sublicenses to the Camurus IP to any of its Affiliates or Third Parties to develop, make, have made, use, sell, offer for sale, market and promote the Product in the Licensed Field in the Territory,

provided, that in each such case, (i) Rhythm shall be liable to Camurus as if Rhythm is exercising such sublicensed rights itself under this Agreement, (ii) the Sublicensee shall be permitted to grant further sublicenses, (iii) Rhythm shall provide upon written request by Camurus reasonable assurance that its Sublicensees are required to comply with confidentiality, indemnity, reporting, audit rights, access to Development Data, and information obligations owed by such Sublicensees to Rhythm that correspond and are no less stringent than the confidentiality, indemnity,

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reporting, audit rights, access to Development Data, and information obligations owed by Rhythm to Camurus as set forth in this Agreement. Rhythm shall promptly provide notice to Camurus of any sublicense granted pursuant to this Section 2.3. Any person or entity that receives a sublicense or is otherwise granted the right to promote and sell the Product as permitted hereunder is a “**Sublicensee**”.

2.4 **Grant Back to Camurus.** Subject to and upon the terms and conditions set forth in this Agreement, Rhythm hereby grants to Camurus, and Camurus hereby accepts, a world-wide, paid up, non-exclusive, perpetual license, with the right to sublicense, under Rhythm Collaboration IP (but excluding Rhythm’s Development Data and regulatory filings, including INDs, NDAs and Regulatory Approvals, which are addressed in Section 3.7), to develop, make or have made, use, sell, offer for sale, market and promote products that are not the Product or a Competing Product, in the Territory. Notwithstanding anything express or implied in the foregoing provisions of this Section 2.4 to the contrary, such license by Rhythm to and/or under Rhythm Collaboration IP shall only include those portions of any Rhythm Collaboration IP that are directly related to the FC Technology and that do not include information concerning the Drug, the Product or any Competing Product or any method of making or using the same. In the event that Camurus sublicenses any of its rights under this Section 2.4, (i) Camurus shall be liable to Rhythm as if Camurus were exercising such sublicensed rights itself under this Agreement and (ii) Camurus shall provide upon written request by Rhythm reasonable assurance that any sublicensee of Camurus’ rights under this Section 2.4 is required to comply with obligations with respect to confidentiality and indemnity owed by such sublicensee to Camurus that correspond and are no less stringent than the obligations owed by Camurus to Rhythm pursuant to this Agreement with respect to confidentiality and indemnity.

3 DEVELOPMENT OF PRODUCT

3.1 **Rhythm Development Responsibility and Diligence.** Rhythm shall have the responsibility for, and have final decision-making authority with respect to, development of the Product at its own cost and Rhythm shall in doing so at all times exercise Commercially Reasonable Efforts to develop the Product through completion of the Ph1B PK/POC Study. If Rhythm elects to continue development of the Product following successful completion of the Ph1B PK/POC Study in accordance with Section 3.6, then Rhythm shall be deemed to have satisfied Rhythm’s obligation to use Commercially Reasonable Efforts to develop the Product. Rhythm shall keep the JDC regularly apprised of the progress of the execution of the Development Plan(s). Both parties recognize that, in general, the Development Plans represent projections only and may be subject to change during the development process. Both Parties also recognize that the development of the Product is being undertaken as a bridge of Rhythm’s efforts to develop the Drug and secure its approval by Regulatory Authorities; accordingly, in the event and to the extent that the primary Drug development program suffers delays or set-backs, those events will have a corresponding effect on efforts under this Agreement with respect to the Product. Rhythm may decide from time to time to update to the Development Plan(s) as necessary to reflect changes in the progress of development

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for the Product. Any proposed change to the Development Plan shall set forth a summary anticipated development activities and timelines for the Product, and propose any responsibility of Rhythm or Camurus (if any) for carrying out any such activities. Rhythm shall also provide to Camurus draft forms of Product protocols for the purpose of obtaining comments. Rhythm shall consider in good faith all comments provided by Camurus within the thirty (30) day period following Camurus receipt of such protocols. Any Clinical Trials shall be conducted by Rhythm in accordance with GCP. If Rhythm elects to continue development of the Product following successful completion of the Ph1B PK/POC Study in accordance with Section 3.6, then Rhythm shall thereafter provide Camurus within sixty (60) days after the end of every second calendar quarter, a reasonably detailed report on progress made toward the development of the Product during such preceding 6-month period, including the status of applications for regulatory approvals until such time as Rhythm becomes obligated to provide Payment Reports pursuant to Section 5.7 in the U.S. or one or more countries within the EU. Rhythm shall be deemed to have satisfied such obligation to provide such reasonably detailed in any calendar year if Rhythm complies with its obligations under Section 3.4(d) hereof with respect to any meeting of the JDC that takes place on any date during such calendar year that is on or prior to the 60th day after the end of the second calendar quarter of such calendar year.

3.2 Camurus Services. Rhythm may utilize Camurus to perform certain agreed development activities as shall be specified in a separate written agreed addendum to the Development Plan. Rhythm shall reimburse Camurus for its costs and expenses incurred in providing such services pursuant to a budget for such costs and expenses, including FTE Costs, which shall be set forth in the addendum to the Development Plan. Such costs and expenses incurred by Camurus may be invoiced to Rhythm on a monthly basis. Rhythm shall effect payment of all invoices to Camurus' designated bank account within thirty (30) days after the date of Camurus' invoice. Camurus shall together with such invoices provide reasonable available supporting documentation of such costs and expenses (including relevant Third Party invoice and specification of hours worked by Camurus and a summary of the work performed). Rhythm agrees not to withhold payment in respect of any Third Party costs that are within an agreed budget, although Rhythm may dispute the same. For clarity, Camurus shall not be obliged to carry out any activities unless Rhythm has agreed to reimburse Camurus the associated costs and expenses.

3.3 Joint Development Committee. Within ten (10) days of the Effective Date, the Parties shall appoint a Joint Development Committee (the "JDC") of four (4) members. Subject to this Section 3.3 and Section 3.4 below, the JDC shall be the primary forum for exchange of information and review of Rhythm's progress in the development and registration of the Product and the JDC shall have the following responsibilities;

- (i) reviewing the progress and results of Rhythm's development efforts;
- (ii) reviewing material amendments or updates to the Development Plan;
- (iii) agreeing procedure for filing of Joint Patents;
- (iv) reviewing the progress of Camurus' technology transfer activities in respect of the Product as detailed in Section 6.2,

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- (v) discuss publications regarding Product (such as abstract presentations at conferences, symposiums), and
- (vi) Camurus will advise the JDC of any material issues that it is observing with respect to the characteristics of its FC Technology that are of potential utility to Rhythm in its development efforts with respect to its clinical and regulatory approach for the Product all to the extent covered by Rhythm's license rights in Section 2.1.

3.4 Meetings of the JDC:

- (a) The JDC shall consist of an equal number of representatives appointed by each of Camurus and Rhythm. Each Party may, with notice to the other, substitute any of its members serving on the JDC and may invite ad hoc non-voting members as desired. The Parties may also, by mutual agreement, increase or decrease the number of members serving on the JDC; provided that the number of members representing each Party remains equal. Rhythm shall have the right to appoint one of its members to be the chairperson of the JDC, whose term shall run for so long as the JDC is in existence.
- (b) The JDC shall meet as necessary but in any event no less frequently than semi-annually. Meetings of the JDC may take place by telephonic or video conference unless otherwise agreed. Minutes from the meetings of the JDC shall be kept by the Chairman of the JDC and circulated to Camurus members within a reasonable time for comments and approval. Minutes shall not become official until approved by both Parties in writing; minutes shall be presented for approval as the first order of business at the subsequent JDC meeting, or if it is necessary to approve the minutes prior to such subsequent meeting, then the Parties shall approve the minutes within thirty (30) days of receipt thereof.
- (c) Each Party shall bear its own costs, including travel and lodging for its personnel serving on the JDC or attending meeting of the JDC.
- (d) Each Party shall submit to the JDC members ten (10) days in advance of each JDC meeting reasonably detailed progress and other reports to keep the JDC informed of the current progress and status of the conduct of its respective activities.
- (e) The quorum for JDC meetings shall be two (2) members, provided there are at least one (1) member from each of Camurus and Rhythm present.

- (f) Information that otherwise falls under the definition of Confidential Information contained in reports made pursuant to Section 3.3 or Section 3.4 will be subject to the confidentiality provisions of Section 8.
- (g) The term for the JDC shall commence on the date it is established by the Parties and continue until the Product receives regulatory approval in the United States or the EU.
- 3.5 Regulatory Filings and Approvals in the Territory. Rhythm shall have the responsibility for, and have final decision-making authority with respect to applying for and obtaining Regulatory Approvals for each Product in the Territory

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which applications and approvals shall be held by and in the name of Rhythm. Camurus shall provide assistance as reasonably requested in (i) compiling an IND and NDA; (ii) providing support for meetings with Regulatory Authorities and (iii) responding to questions from the Regulatory Authorities on technical (as opposed to pricing) questions on the Product and Camurus shall be reimbursed for such work at Camurus FTE Costs and reimbursement of documented expenses. Rhythm shall pay all user fees and other costs required to obtain and maintain such Regulatory Approvals.

- 3.6 Decision Not To Proceed After Ph1B PK/POC Clinical Trial. Without limiting the generality of the foregoing, on a Product-by-Product basis, Rhythm shall use Commercially Reasonable Efforts to perform the development activities through the completion of the first Ph1B PK/POC Clinical Trial with the Product as set forth in the Development Plan (the “**Ph1B PK/POC Study**”). Within ninety (90) days following receipt of the final report from the Ph1B PK/POC Study Rhythm shall make a determination whether or not to proceed with development. If Rhythm elects to proceed with further development following a successful Ph1B PK/POC Study then Rhythm shall thereafter provide Camurus with the semi-annual reports described in Section 3.1 (last sentence). If Rhythm elects to proceed with further development that constitutes re-performance of a Ph1B PK/POC Study on an alternative formulation of the Product that was the subject of an unsuccessful Ph1B PK/POC Study then Rhythm shall provide Camurus with an updated Development Plan covering subsequent development activities through the re-performance of such Ph1B PK/POC Study within sixty (60) days of the date it notifies Camurus of its decision to re-perform a Ph1B PK/POC Study. If Rhythm elects not to proceed with any additional development then Rhythm shall notify Camurus of such decision and terminate this Agreement in accordance with Section 11.3(e). If Rhythm fails to deliver notice to Camurus of Rhythm’s decision to proceed with development or to terminate development within the 90-day period specified above then Camurus may terminate this Agreement as set forth in Section 11.3(e). Notwithstanding anything to the contrary herein, if Rhythm has not initiated dosing in the first Phase III study with the Product within []* from the completion of the Ph1B PK/POC Study then Rhythm shall be required to terminate the Agreement in accordance with Section 11.3(e) and if Rhythm fails to terminate the Agreement then Camurus may terminate this Agreement as set forth in Section 11.3(e); provided, however that where Rhythm’s failure to meet the foregoing []* deadline results from any documented safety issues, manufacturing process issues, changes to legal requirements or requests from a Regulatory Authority, in each case to the extent outside Rhythm’s control, then as long as Rhythm uses commercially reasonable efforts to overcome such issues, Rhythm shall not be required to terminate the Agreement as provided above in this Section 3.6 and Camurus shall not have the right to terminate the Agreement as provided above in this Section 3.6.

- 3.7 Development Data. To the extent permitted by law and subject to the terms and conditions set forth in this Section 3.7, Rhythm grants Camurus, its Affiliates and licensees the right to cross-reference those portions of any Development Data and regulatory filings, including INDs, NDAs and Regulatory Approvals, Controlled by Rhythm or its Affiliates that are directly related to safety and CMC aspects of the FC Technology and do not include information concerning the Drug and that have

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been submitted to the FDA or any other applicable Regulatory Authorities, in each case only to the extent that such right to cross-reference, is necessary or useful for Camurus’, its Affiliates’ and licensees’ regulatory filings for other products that utilize the FC Technology, provided that such other products do not consist of a Product or a Competing Product. Camurus shall provide Rhythm with at least thirty (30) days advanced written notice of the regulatory agency and division which is receiving the cross-reference filing, before Camurus or any of its Affiliates or licensees exercises any right of cross-reference as contemplated under the foregoing provisions of this paragraph. Rhythm shall give Camurus, its Affiliates and licensees reasonable access and right to use (including the right to copy where reasonably required) to a copy of those portions of the Development Data, IND, NDA or Regulatory Approvals Controlled by Rhythm, its Affiliates or its Sublicensees that are directly related to safety and CMC aspects of the FC Technology and do not include information concerning the Drug , in each case only to the extent that such right of reasonable access and use is necessary or useful for development or regulatory filings for products that utilize the FC Technology and do not consist of a Product or a Competing Product. Camurus shall be responsible for reimbursement to Rhythm of any costs on an hourly fee basis incurred in connection with the provision of access to any data by Rhythm pursuant to this Section 3.7, including the costs of segregating data that relates solely to the FC Technology. Such costs shall be calculated on an hourly fee basis.

Camurus shall provide Rhythm, its Affiliates, Sublicensees with a right of cross-reference, a right of reasonable access and a right to use the development data and regulatory filings and regulatory approvals that Camurus or its Affiliates Control that are directly related to the FC Technology and that do not include information concerning any active pharmaceutical ingredient under development by Camurus or its Affiliates or licensees or sublicensees, in each case only to the extent that such right to cross-reference, such right of reasonable access and such right of use is necessary or useful for regulatory filings for the Product made or to be made by Rhythm, its Affiliates or Sublicensees. Rhythm shall provide Camurus with at least thirty (30) days advanced written notice of the regulatory agency and division which is receiving the cross-reference filing,

before Rhythm or any of its Affiliates or Sublicensees exercises any right of cross-reference as contemplated under the foregoing provisions of this paragraph. Rhythm shall be responsible for reimbursement to Camurus of any costs incurred in connection with the provision of access to any data by Camurus pursuant to this Section 3.7, including the costs of segregating data that relates solely to the FC Technology. Such costs shall be calculated on an hourly fee basis. It is noted that Camurus is currently negotiating sublicensing rights under its license agreement with []* to []* generated know-how pertaining to the FC Technology and that do not include information concerning any active pharmaceutical ingredient under development by []* or its Affiliates. The Parties agree that until Camurus succeeds in securing such sublicensing rights from []* under such license agreement that would permit Camurus to grant to Rhythm rights to such know-how as provided in Section 3.7, Camurus shall not sublicense or otherwise grant or provide the rights granted by Rhythm to Camurus in this Section 3.7 or Section 2.4 to []* or its Affiliates.

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- 3.8 **Reporting Adverse Events:** Rhythm shall be responsible for reporting all adverse events (as defined in the then current edition of ICH Guidelines and any other relevant regulations or regulatory guidelines or any other safety problem of any significance, hereafter “Adverse Events”) relating to the Product to the appropriate regulatory authorities in the countries in the Territory in accordance with the appropriate laws and regulations of the relevant countries and authorities. Rhythm shall ensure that its Affiliates and Sublicensees comply with all such reporting obligations. In the event that Rhythm knows or acquires knowledge that any Adverse Event relating to the Product is attributable to the FC Technology and is not attributable to the Drug, then Rhythm shall provide prompt written notice of such Adverse Event to Camurus. In addition, at each meeting of the JDC, a representative of Rhythm shall present to the JDC, and the JDC shall review, all Adverse Event relating to the Product that have occurred since the last meeting of the JDC

4 COMMERCIALIZATION

- 4.1 **Responsibility.** Rhythm shall have responsibility for, and final decision-making authority with respect to, commercialization of Products in the Territory at its own cost.

- 4.2 **Reserved.**

- 4.3 **Reserved.**

- 4.4 **Reserved.**

- 4.5 **Reserved.**

5 PAYMENT OBLIGATIONS

- 5.1 **Signing Fee.** Within the later to occur of (i) five (5) Business Days of the Effective Date and (ii) five (5) Business Days after receipt of an invoice from Camurus, Rhythm shall pay Camurus a non-refundable and non-creditable signing fee of []* US Dollars (US\$[]*) payable by wire transfer of immediately available funds to an account designated in writing by Camurus.

- 5.2 **Milestone Payments.** On a Product-by-Product basis, Rhythm shall pay the following non-refundable, non-creditable amounts upon the achievement of the following events, within the later to occur of (i) sixty (60) calendar days after each such event and (ii) ten (10) Business Days after receipt of an invoice from Camurus for the milestone payment due with respect to each such event:

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MILESTONE EVENT	MILESTONE PAYMENT
Upon completion (i.e. release of first eGMP batch of Product) of tech transfer and IND support for the filing of the first IND for the Ph1B PK/POC Study but in no event later than upon filing of said IND.	US\$ []*.
Successful completion of the Ph1B PK/POC Study. Successful completion shall be deemed to have occurred if, after completion of the Ph1B PK/POC Study, Rhythm pursues additional development activities in preparation for the commencement of a Phase II Study. If, after completion of the Ph1B PK/POC Study, Rhythm does not pursue development activities in preparation for the commencement of a Phase II Study, Rhythm must within 90 days from completion of the Ph1B PK/POC Study (i) treat the Ph1B PK/POC Study as successfully completed and pay the associated \$[]* Milestone Payment to Camurus, (ii) renegotiate and agree with Camurus as to the extent of Rhythm’s obligation, if any, to have to pay	US\$ []*.

the \$[]* Milestone Payment Milestone Payment associated with successful completion of the Ph1B PK/POC Study or (iii) terminate this Agreement as set forth in Section 11.3(e). Nothing in this paragraph shall be construed as requiring that any Milestone Payment be paid or payable more than once upon the first achievement of the applicable Milestone and any renegotiated Milestone Payment under this paragraph shall be in lieu of the \$[]* Milestone Payment payable by Rhythm to Camurus upon successful completion of the Ph1B PK/POC Study with the Product.

First dosing of the Product in the first Phase III Clinical Trial. US\$ []*.

Filing of the first NDA for the Product in the United States. US\$ []*.

First NDA Approval for the Product in the United States. US\$ []*.

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Filing of the first NDA for the Product in the EU. US\$ []*.

First NDA Approval for the Product in the EU. US\$ []*.

In no event shall any development or approval milestone payment be payable more than once for each Product and in no event shall the aggregate amount of all development and approval milestone payments payable with respect to each Product exceed US\$[]*.

5.3

Royalties.

On a Product-by-Product basis, Rhythm shall pay to Camurus royalties (“**Royalties**”) equal to the percentages on the below annual Net Sales of Product in the Territory as described below.

Product Net Sales Tier	Royalty
For the portion of aggregate annual Net Sales of Product of less than []* in the Territory	[]*%
For the portion of aggregate annual Net Sales of Product equal to or greater than []* and less than []* in the Territory	[]*%
For the portion of aggregate annual Net Sales of Product equal to or greater than []* and less than []* in the Territory	[]*%
For the portion of aggregate annual Net Sales of Product equal to or greater than []* in the Territory	[]*%

Royalties shall be payable for a time period calculated on a Product-by-Product and country-by-country basis in respect of the licenses granted to Rhythm by Camurus hereunder beginning on the First Commercial Sale of such Product in such country and ending on the later of (a) ten (10) years after the date of such First Commercial Sale of such Product in such country and (b) the expiration of the last to expire Valid Claim covering such Product within (i) Camurus Platform Patents or (ii) Patent Rights claiming Collaboration Inventions, in such country. The period during which Royalties are payable in respect of a Product in any country is referred to as the “**Royalty Term**”. Notwithstanding the foregoing, royalty rates shall be reduced by []*% with respect to sales of a Product in any country of the Territory during the Royalty Term if the sale, manufacture or use of the Product in such country is not covered by any Valid Claim within (1) the Camurus Platform Patents or (2) Patent Rights covering Collaboration Inventions and in each case there is a Generic

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Product sold in such country. In no event may the Royalties set forth first above in this Section 5.3 be reduced by more than []*% by application of one or more royalty reduction provisions in this Agreement.

5.4

Sales Milestones. Rhythm shall pay the following non-refundable, non-creditable sales milestones upon the achievement of the following sales levels for all Products in the Territory. Payment for any such milestones shall be made within the later to occur of (i) sixty (60) calendar days after the achievement of the applicable milestone and (ii) ten (10) Business Days of receipt of appropriate original invoice from Camurus. Sales milestones will be paid in accordance with the schedule below, with each milestone paid only once and on the first occurrence of the event, as set forth below. In the event more than one sales milestone is reached in the same year, then each such milestone shall be due that year.

Product Event	Amount

When Net Sales of a Product in the Territory first exceed US\$[calendar year]* in a	US\$[]*
When Net Sales of a Product in the Territory first exceed US\$[calendar year]* in a	US\$[]*
When Net Sales of a Product in the Territory first exceed US\$[calendar year]* in a	US\$[]*
When Net Sales of a Product in the Territory first exceed US\$[calendar year]* in a	US\$[]*

In no event shall sales milestone payments be payable in excess of US\$[
]*.

5.5

Third Party Licenses. If Rhythm, to avoid infringement of Third Party Patent Rights in connection with the Product, to the extent such infringement relates the use of Camurus IP, obtains a license under an issued patent(s) from such Third Party in any country in the Territory to make or have made, use, offer to sell, sell, have sold, import, or otherwise exploit a Product pursuant to the licenses granted hereunder, then Royalties calculated on Net Sales of such Product in such country shall, subject to Section 5.3, be offset by [
]* of any royalties paid by Rhythm as and when paid to such Third Party under such Third Party license. For the avoidance of doubt, payments to such Third Party that may be offset shall be limited to such payments allocable to the license of such technology (excluding, for example, any payments in respect of development services or the supply of products) and allocable to the Product (excluding, for example, other uses of such technology by Rhythm). Rhythm shall provide Camurus with copies of the relevant terms of such license agreement with such Third Party and other material information in its possession in respect of such technology subject to Camurus undertaking confidentiality in respect of such disclosures by Rhythm. Rhythm shall consult with Camurus prior to entering into any such license agreement and provide Camurus a reasonable opportunity to provide its views on the need or benefit to obtain such license and the financial and other terms thereof. If Rhythm exercises

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its right in Section 5.6 to buy down Royalties, then Rhythm's rights to offset future royalties paid to Third Parties as provided in this Section 5.5 shall cease.

5.6

Royalty Buy-Down. Rhythm shall have the right on a Product-by-Product basis, exercisable at any time during a period beginning on the First Commercial of the applicable Product and ending on the [
]* anniversary thereof, to buy down the Royalties to a flat rate of [
]* on Net Sales of such Product by making payment to Camurus of a one-time non-refundable and non-creditable amount of [
]*. The reduced royalty rate shall apply to all Net Sales of such Product from the calendar quarter following the calendar quarter in which said lump-sum payment is received by Camurus. Any sales milestones that would otherwise become due pursuant to Section 5.4 after the calendar quarter in which said payment was received by Camurus, shall no longer be payable.

5.7

Royalty and Milestone Reports. Royalty payments shall be paid within sixty (60) calendar days after the first day of January, April, July and October of each year following the First Commercial Sale of a Product, and shall include a written report with respect to the preceding quarter (the "**Payment Report**") stating: (a) the gross sales and number of units sold of each presentation of the Product sold by Rhythm, its Affiliates and Sublicensees in each country in the Territory; (b) Net Sales of the Product sold by Rhythm, its Affiliates and Sublicensees, during such quarter on a country-by-country basis; (c) the date of any First Commercial Sale of the Product in each country during such quarter, (d) currency exchange rates used in determining the Royalties and (e) a calculation of the amounts due to Camurus. Rhythm shall notify Camurus in writing within sixty (60) calendar days after the achievement of any milestone described in Section 5.2 or Section 5.4.

5.8

Payments.

- (a) All payments due under this Agreement shall be paid in immediately available funds in US Dollar to the bank account designated in writing by Camurus, as the case may be. To the extent Net Sales are accrued in currencies other than US Dollar, Net Sales shall be converted to US Dollar, as the case may be, at the average daily rate of exchange for the applicable calendar quarter as published by Financial Times (UK edition). The calculation of the average rate of exchange shall be stated in terms of US Dollar per foreign currency units.
- (b) All payments hereunder are exclusive of any taxes, fees or charges imposed by any local or national authority. In the event that Rhythm reasonably determines that any tax, duty or other levy is required to be paid or withheld on account of Royalties or other payments payable to Camurus under this Agreement, Rhythm shall make such withholding payments as required and subtract such withholding payments from the payments to be made to Camurus as set forth in this Section 5, or, if applicable, Camurus will reimburse Rhythm or its designee(s) for the amount of such required withholding payments that are not subtracted from the payments made to Camurus as set forth in this Section 5, within fifteen (15) days of notice to Camurus. Rhythm shall provide Camurus with documentation of such withholding and payment in a manner that is satisfactory for purposes of reporting to the U.S. Internal Revenue Service. Any withholdings paid by Rhythm shall be for the benefit of Camurus.

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- (c) Any payments that are not paid within the date such payments are due under this Agreement shall bear interest at an annual rate of interest equal to the London Interbank Offered Rate (“LIBOR”), plus five (5) percentage points, calculated on the number of days such payment is delinquent.

5.9 **Books and Records; Audit Rights.** Rhythm shall keep full and true books of accounts and other records in sufficient detail so that the Royalties payable hereunder can be properly ascertained. Rhythm shall, at the request of Camurus, permit a nationally recognized independent certified public accountant selected by Camurus and reasonably acceptable to Rhythm to have access during ordinary business hours, to such books and records as may be necessary to determine the correctness of any Payment Report or payment made under this Agreement or to obtain information as to Royalties and milestones payable in case of failure to report or pay pursuant to the terms of this Agreement. The auditor shall execute a written confidentiality agreement with Rhythm and shall disclose to Camurus only the amount and accuracy of payments reported and actually paid or otherwise payable under this Agreement. The auditor shall send a copy of the report to Rhythm at the same time it is sent to Camurus. Such examination shall be conducted (a) after at least thirty (30) days prior written notice from Camurus, (b) at the facility(ies) where such books and records are maintained, and (c) no more frequently than once in any calendar year or more than once with respect to a particular year. Camurus shall be responsible for expenses for the independent certified public accountant, except that Rhythm shall reimburse Camurus in full thereof if the independent accountant determines the Royalties and milestones paid by Rhythm to Camurus are less than ninety-five percent (95%) of the amount actually owed for the period of the audit. As a condition to any sublicense granted by Rhythm hereunder, Rhythm shall ensure that Camurus has the same audit rights as those described in this Section 5.9 with respect to any such Rhythm Affiliate or Sublicensee.

6 MANUFACTURE

6.1 **Identification of CMO.** Rhythm shall have responsibility for, and final decision-making authority with respect to, the manufacture of Product for non-clinical, clinical and commercial use and sale in the Territory. Rhythm, or its designated CMO as applicable, shall be EU and US GMP approved and able to manufacture according to the Regulatory Approvals in the applicable countries in the Territory. Until the tech transfer process to Rhythm or its CMO has been successfully completed as set forth in Section 6.2, Camurus may procure such supply of Rhythm’s non-commercial requirements of Product from Camurus’ existing CMO at Camurus’ Manufacturing Cost. In such case, the Parties shall enter into separate supply agreements governing the terms and conditions of such non-commercial supply from Camurus’ CMO to Rhythm and shall use good faith efforts to negotiate and enter into the foregoing within one hundred and twenty (120) days from the Effective Date.

6.2 **Technology Transfer.** Camurus shall use Commercially Reasonable Efforts to provide such of its manufacturing technology as may be reasonably necessary to enable Rhythm or its designated CMO to manufacture the Product for non-clinical, clinical and commercial use, and shall use Commercially Reasonable Efforts to

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provide technical assistance to enable the use of such manufacturing technology to manufacture the Product. Prior to such technology transfer, the Parties will agree upon a technology transfer plan and corresponding budget. Rhythm shall reimburse Camurus its out of pocket costs and expenses as well as Camurus’ FTE Costs incurred in providing such technology transfer and technical assistance. Camurus shall be reimbursed by Rhythm on a monthly basis, within thirty (30) days of receipt of an invoice setting forth such costs and expenses.

6.3 **Rhythm Supply Agreement.** If Rhythm uses a CMO, as soon as commercially possible Rhythm shall enter into one or more Rhythm Supply Agreements with the CMO covering the tech transfer, process development, scale-up and manufacture of Product.

7 INTELLECTUAL PROPERTY

7.1 Trademarks.

- (a) Rhythm shall have the right to select, and shall register and maintain, at its expense, such Product Trademarks as shall be used for the promotion, marketing and sale of the Product in the Territory. Rhythm shall own such Product Trademarks and all goodwill associated therewith.
- (b) Rhythm may use the Camurus Trademark for commercialization of Product in the Territory. If Rhythm opts to use the Camurus Trademark, save to the extent Rhythm may be required to do so by a Regulatory Authority or pursuant to the requirements of a Regulatory Approval, Rhythm shall not conceal or otherwise obscure, remove or otherwise interfere with the Camurus Trademark. Rhythm shall not register or use any Trademark confusingly similar to any Camurus Trademark or any other Trademarks used by Camurus with the FC Technology. Rhythm shall ensure that each reference to and use of the Camurus Trademark in any marketing material related to Product is accompanied by an acknowledgement that the Camurus Trademark is owned by Camurus and used by Rhythm under license. Rhythm shall adhere to any reasonable requests from Camurus relating to Rhythm’s use of the Camurus Trademark.

7.2 **Ownership of Collaboration Inventions.** Subject to the terms hereof, including the licenses and other rights granted hereunder, all Collaboration Inventions shall be owned as follows:

- (a) All Collaboration Inventions, including Joint Inventions, relating specifically to [*], shall be exclusively owned by Camurus.
- (b) All Collaboration Inventions, including Joint Inventions, relating specifically to [*], shall be exclusively owned by Rhythm.
- (c) The ownership of Collaboration Inventions not owned by Camurus or Rhythm in accordance with Section 7.2(a) or Section 7.2(b) shall be determined with reference to inventorship under U.S. patent law. If the Parties fail to agree with respect to inventorship, the dispute will be referred to a Third Party U.S. patent attorney acceptable to each of the Parties for Expert Determination as provided in Exhibit 7.2(c). The Parties shall jointly own all Collaboration Inventions that are

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Joint Inventions, other than those covered in Section 7.2(a) or Section 7.2(b), and, subject to the rights granted each Party under this Agreement, each Party may use, sell, keep, license or assign its interest in Joint Inventions and otherwise undertake all activities a sole owner might undertake with respect to such Joint Inventions, without the consent of and without accounting to the other Party. “**Joint Inventions**” means Collaboration Inventions for which it is determined, in accordance with the patent law of the United States, that both: (i) one or more employees, consultants or agents of Camurus or any other persons obligated to assign such Collaboration Invention to Camurus; and (ii) one or more employees, consultants or agents of Rhythm or any other persons obligated to assign such Collaboration Invention to Rhythm, are inventors of such Collaboration Invention. For any Joint IP that could be the subject of an application for a Patent Right, each Party, in conjunction with such Party’s patent counsel will make an initial determination of inventorship prior to filing the application therefor to confirm that it is Joint IP. Each Party will provide information and records relevant to such determination to the other Party and such patent counsel

- (d) Subject to appropriate confidentiality undertakings, each Party shall promptly notify the other Party when it learns a Collaboration Invention has been made and promptly after the completion of invention disclosure statements for such Collaboration Invention (or, if any provisional or other patent applications are filed claiming such invention, promptly after such filing), and, to the extent a Party is granted rights hereunder in such Collaboration Invention, shall provide a copy of the same to the other Party.
- (e) For the avoidance of doubt, neither Party is granted any license rights to any intellectual property rights of the other Party, which may be required for such Party to use a Collaboration Invention, unless otherwise expressly granted herein.
- (f) Each of the Parties shall do all such acts and things and execute all such deeds and documents as may be necessary or desirable for them to perfect their rights of ownership as specified in this Section 7.2 and otherwise implement the provisions of this Section 7. Each Party shall, and shall cause its applicable Affiliates, Third Party subcontractors, and their respective employees and agents to, perform at the requesting Party’s cost all reasonable acts reasonably requested, including the execution of confirmatory deeds and assignment documents of Patent Rights as may be necessary or desirable for them to perfect their title therein in accordance with the forgoing provisions of this Section.

7.3

Prosecution of Patents.

- (a) Patent Prosecution of Camurus IP. Camurus shall control the Prosecution of the Patent Rights within Camurus Platform IP (“**Camurus Platform Patents**”) at its own cost and expense using Commercially Reasonable Efforts to Prosecute all patent applications forming part of Camurus Platform Patents to grant with Valid Claims, including conducting any necessary or desirable oral or written proceedings. Camurus shall provide Rhythm with a copy of each new draft application and replies to substantive office actions within the Camurus Platform Patents (including, for clarity, divisional and continuation applications), and shall keep Rhythm informed of all material developments in relation to Camurus

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Platform Patents and shall provide Rhythm with copies of relevant documents related to the Prosecution of Camurus Platform Patents in the United States and EU and any PCT application. Camurus shall provide relevant documents related to the Prosecution of the Camurus Platform Patents in all other countries in the Territory upon request from Rhythm. In the event that, having filed, Camurus declines to further Prosecute any Camurus Platform Patents in any country of the Territory, Camurus shall provide Rhythm with written notice thereof. Such notice shall be given at least sixty (60) days prior to the expiration of any official substantive deadline relating to such activities. In any such circumstances and provided that no earlier licensee of Camurus has assumed the right to Prosecute such Camurus Platform Patents Rhythm shall have the right to decide that Rhythm should continue to Prosecute such Camurus Platform Patents owned by Camurus at Rhythm’s expense and in such case Rhythm shall give written notice to Camurus; provided that if Camurus’ decision to decline to further Prosecute any pending Camurus Platform Patents is as a result of the withdrawal of an unpublished patent application and the reason for such withdrawal was to enable the filing of another patent application claiming the same inventions, Rhythm shall not have the right to decide that Rhythm should continue to Prosecute the withdrawn unpublished patent application. Camurus shall upon receipt of any such notice from Rhythm transfer to Rhythm copies of all of its files relating to the relevant Camurus Platform Patents and at Rhythm’s reasonable cost and expense execute any documents to otherwise transfer control of such Prosecution to Rhythm. Camurus shall remain the owner of such Camurus Platform Patents and Rhythm shall provide Camurus the same information and rights required under this Section 7.3(a) to be provided Rhythm concerning the Prosecution of such Camurus Platform Patents. Rhythm may deduct the prosecution costs with respect to such Camurus Platform Patents from the royalties payable to Camurus under this Agreement. This Section 7.3 (a) shall apply mutatis mutandis to Patent Rights within Collaboration Inventions solely owned by Camurus pursuant to Section 7.4.

- (b) Patent Prosecution of Collaboration Product Patents and Rhythm Product Patents in the Territory. Rhythm shall control the Prosecution of (i) the Patent Rights to any and all Collaboration Inventions owned by Rhythm pursuant to Section 7.2(b), Section 7.2(c) if solely owned by Rhythm or Section 7.4 (jointly “**Collaboration Product Patents**”), and (ii) the Rhythm Product Patents, in the Territory at Rhythm’s expense using Commercially Reasonable Efforts to Prosecute all patent applications forming part of the Collaboration Product Patents to grant with Valid Claims, including conducting any necessary or desirable claims or oral or written proceedings. With respect to the Collaboration Product Patents, Rhythm shall provide Camurus the same information and rights required under Section 7.3(a) to be provided Rhythm concerning the Prosecution of the Camurus Platform Patents. In the event that, having filed, Rhythm declines to further Prosecute any Collaboration Product Patents in any country in the Territory, Rhythm shall provide Camurus with written notice thereof. Such notice shall be given at least sixty (60)

days prior to the expiration of any official substantive deadline relating to such activities. In any such circumstances Camurus shall have the right to decide that Camurus should continue to Prosecute such Collaboration Product Patents at Camurus' expense and in such case Camurus shall give written notice to Rhythm. Rhythm shall upon receipt of any

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such notice from Camurus transfer to Camurus all of its files relating to the relevant Collaboration Product Patents and at Camurus' reasonable cost and expense execute any documents to otherwise transfer control of such Prosecution to Camurus. Rhythm shall remain the owner of such Collaboration Product Patents and Camurus shall provide Rhythm the same information and rights required to be provided Camurus under this Section 7.3(b) concerning the Prosecution of such Collaboration Product Patents.

- (c) Joint Patents. With respect to the Prosecution of patent applications claiming Joint Inventions subject to Section 7.2(c) ("Joint Patents"), Rhythm shall have the right to take such actions as are necessary or appropriate to Prosecute Joint Patents at its sole expense; *provided*, that all such patent applications and patents shall be owned jointly. Rhythm shall furnish Camurus with copies of such Joint Patents and other related correspondence relating to such Joint Inventions to and from patent offices throughout the Territory and permit Camurus to offer its comments thereon before Rhythm makes a submission to a patent office. Rhythm shall inform Camurus of the countries in which it intends to file patent applications. Camurus shall offer its comments promptly, including any request that the patents be filed in additional countries; *provided*, that Rhythm shall determine the appropriate action after considering in good faith any comments or requests from Camurus, and *further provided* that in the event that delay would jeopardize any potential patent right, Rhythm shall have the right to proceed without awaiting Camurus' comments. If Rhythm determines in its sole discretion not to Prosecute any patent or patent application within the Joint Patents in any country, and provided that no other patent applications or patents claiming the same or similar subject matter are then pending or issued in that same country, then Rhythm shall provide Camurus with sixty (60) days prior written notice (or such shorter time period that would permit Camurus a reasonable opportunity to respond in a timely manner) of such determination and Camurus shall have the right and opportunity to Prosecute such patent application or patent on behalf of the Parties at Camurus' sole cost and expense. Camurus shall provide Rhythm the same information and rights required under this Section 7.3(c) to be provided Camurus concerning the Prosecution of such Joint Patents.
- (d) As promptly as practicable after the Effective Date (but in no event later than one hundred and twenty (120) days after the Effective Date), Rhythm shall file a patent application with the United States Patent and Trademark Office []*. Camurus shall provide Rhythm with such information and/or invention disclosures reasonably requested by Rhythm, and shall otherwise cooperate with all reasonable requests made by Rhythm, in connection with the preparation, filing and prosecution of such patent application. Notwithstanding anything express or implied anywhere else in this Agreement, all of the inventions claimed in such patent application (other than those of such inventions that are already owned solely by Rhythm as of the Effective Date) shall be deemed and treated, for all purposes of this Agreement, as Collaboration Inventions that are owned solely by Rhythm pursuant to Section 7.2(b) hereof. For clarity, such patent application and all other Patent Rights related to those inventions that are deemed and treated, for all purposes of this Agreement, as Collaboration Inventions shall be deemed and treated as Collaboration Product Patents for all purposes of this Agreement and be subject *inter alia* to Section 7.3 (b).

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- (e) Each Party shall at the expense of the requesting Party execute such documents and take such other actions as may be reasonably requested by the other Party in conjunction with prosecution of patents pursuant to this Section 7.3.
- 7.4 Camurus Platform Patents and Collaboration Product Patents. If, after the Effective Date, any Collaboration Invention relates both to []*, on the one hand, and []*, on the other hand, and patent claims can be made based on the same data, Patent Right or study result, where appropriate Camurus shall, in consultation with Rhythm, file separate patent applications on the same day to any aspect relating to []*, on the one hand, and []*, on the other hand, separately. Any such applications relating specifically to []* shall become part of the Rhythm Collaboration IP and, therefore, shall be exclusively owned by Rhythm, and any such applications relating to []* shall become part of Camurus Platform IP hereunder and, therefore, shall be exclusively owned by Camurus. In the event that the provisions of this Section 7.4 are applicable to any Collaboration Invention, the provisions of this Section 7.4 shall be applied to such Collaboration Invention before the provisions of any of Section 7.2(a) or Section 7.2(b) are given effect with respect to such Collaboration Invention.
- 7.5 Employee Assignment. Each Party shall ensure that any employee of that Party involved in the performance of this Agreement shall be employed on legally binding written terms which require the assignment of all Patent Rights and Know-How resulting from work carried out by that employee to the employing Party. Each Party shall be responsible for all payments to its employees or others in respect of obtaining rights to any such Patent Rights and Know-How.
- 7.6 Patent Term Extensions. For all patents within any Patent Rights relating to or claiming a Product for which NDA Approval has been obtained, the Parties shall use reasonable efforts, in each country where NDA Approval for a Product has been obtained and the law of such country permits application for a patent term extension (or any supplementary certificate), to apply for a patent term extension (or any supplementary certificate) for one or more selected patent within such Patent Rights chosen at Rhythm's reasonable discretion with respect to the Territory. Each Party agrees to cooperate with the other Party in the exercise of the authorizations granted under this Section, and to execute such documents and take such additional action as the other Party may reasonably request in connection therewith.
- 7.7 Third Party Intellectual Property. Each Party shall bring to the attention of the other Party all information regarding potential infringement or misappropriation of Third Party Patent Rights as a result of the manufacture, use, importation, offer for sale, or sale of Product in the Territory.

The Parties shall discuss such information and decide how to handle the matter. This Section 7.7 shall not be interpreted as placing on either Party a duty of inquiry regarding Third Party Intellectual Property rights beyond what is customary for the industry.

- 7.8 **Third Party Infringement.** In the case where either Party believes that the development, manufacture, use or sale of the Product or a Competing Product by a Third Party in the Licensed Field infringes any Camurus Platform Patents, any other Patent Rights licensed by Camurus to Rhythm pursuant to this Agreement,

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any other Collaboration Product Patents covering the Product (including any method of making or using the same) or the Joint Patents (each, an “**Infringing Activity**”), such Party shall disclose full details of the potential infringement to the other Party. In addition, if either Party believes that development, manufacture, use or sale of the Product or a Competing Product by a Third Party in the Licensed Field infringes any other Patent Rights covering the Product, such Party shall disclose full details of the potential infringement to the other Party. The right to prosecute Infringing Activity pursuant to this Agreement is set out in either Section 7.9 or Section 7.10, as applicable. If the Parties fail to agree with respect to whether an Infringing Activity is subject to Section 7.9 or Section 7.10, the dispute will be referred to a Third Party U.S. patent attorney acceptable to each of the Parties for Expert Determination as provided in Exhibit 7.2(c). For the avoidance of doubt, it is understood and agreed that in this section 7.8 and in Section 7.9, Patent Rights claiming the Product do not include Rhythm Product Patents or any other Patent Rights owned or Controlled by Rhythm (other than Collaboration Product Patents).

- 7.9 **Enforcement with respect to Collaboration Product Patents and Joint Patents.** Where an infringement of (x) any Patent Rights specifically claiming the Product (including any method of making or using the same) or (y) any Joint Patents by an Infringing Activity occurs in one or more countries of the Territory, Rhythm shall have the first right to, but shall not be obliged to, at its own cost and expense enforce the same in accordance with the below subparagraphs (i) to (iii).

(i) Rhythm shall have sole conduct of the claim and any proceedings including any counterclaim for invalidity or unenforceability or any declaratory judgment action and including the right to settle. Where Rhythm decides to commence proceedings in relation to any such Patent Rights claiming specifically the Product (including any method of making or using the same) or any Joint Patents it shall be entitled to require Camurus to join Rhythm as co-plaintiff and Camurus shall have the right to join as co-plaintiff. In such case Camurus shall provide all necessary assistance to Rhythm in relation to any such proceeding and Rhythm shall on demand by Camurus pay or promptly reimburse Camurus for the costs of such activity unless Camurus elects to be separately represented (which shall be at Camurus’ discretion), in which case such separate representation shall be at Camurus’ cost and expense;

(ii) if Rhythm succeeds in any such infringement proceedings whether at trial or by way of settlement, the proceeds of any award or damages or settlement in respect of such infringement proceedings shall first be applied to reimburse (a) an amount equal to Rhythm’ costs of taking the proceedings and (b) an amount equal Camurus’ costs, with the remainder being retained by Rhythm less []* per cent []* thereof, which amount shall be paid to Camurus;

(iii) if Rhythm fails to take any such proceedings in respect of any such Patent Rights claiming specifically the Product (including any method of making or using the same) or any Joint Patents in the Territory, Camurus may give Rhythm written notice requesting Rhythm to take such proceedings within thirty (30) days of the date of notice and if Rhythm fails to take such action within said period, Camurus shall, subject to the prior written consent of Rhythm, be entitled to do so at its own cost and expense. If Rhythm gives such consent then Camurus shall be entitled to

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require Rhythm to join Camurus as co-plaintiff and Rhythm shall have the right to join as co-plaintiff. In such case, Rhythm shall provide all necessary assistance to Camurus in relation to such proceedings and Camurus shall on demand by Rhythm pay or promptly reimburse Rhythm for the costs of such activity, unless Rhythm elects to be separately represented (which shall be at Rhythm’ discretion), in which case such separate representation shall be at Rhythm’s cost and expense. If Camurus succeeds in any such proceedings, the proceeds of any award or damages or settlement in respect of such proceedings shall first be applied to reimburse (a) an amount equal to Camurus’ costs of taking the proceedings and (b) an amount equal Rhythm’ costs referred to in this Section 7.9(iii), with the remainder being retained by Camurus, less []* per cent []* thereof, which amount shall be paid to Rhythm. Camurus shall not enter into a settlement, consent judgment or other voluntary final disposition of an action or claim or counterclaim under this Section 7.9 without the prior written approval of Rhythm, such consent not to be unreasonably withheld. For the avoidance of doubt, it is understood and agreed that in this Section 7.9, Patent Rights specifically claiming the Product (including any method of making or using the same) do not include Rhythm Product Patents or any other Patent Rights owned or Controlled by Rhythm (other than Collaboration Product Patents).

- 7.10 **Enforcement with respect to Camurus Platform Patents.** Where an infringement of Camurus Platform Patents not specifically claiming the Product (including any method of making or using the same) by an Infringing Activity is occurring in one or more countries of the Territory, Camurus shall have the right, but shall not be obliged, at its own cost and expense to enforce the same. Camurus shall be entitled to require Rhythm to join Camurus as co-plaintiff. In such case Rhythm shall provide all necessary assistance to Camurus in relation to any such proceeding and Camurus shall on demand by Rhythm pay or promptly reimburse Rhythm for the costs of such activity. If Camurus succeeds in any such infringement proceedings whether at trial or by way of settlement, the proceeds of any award or damages or settlement in respect of such infringement proceedings shall first be applied to reimburse (a) an amount equal to Camurus’ costs of taking the proceedings and (b) an amount equal Rhythm’s costs, if any, with the remainder being retained by Camurus less []* per cent []* thereof, which amount shall be paid to Rhythm.

Camurus shall have the sole right to settle such proceedings, provided that such settlement does not include a license or covenant not to sue under the Camurus Platform IP or causes Rhythm to incur any losses in which case Rhythm's consent to the terms of such license shall be required, such consent not to be unreasonably withheld, conditioned or delayed. If Camurus elects not to enforce any such Camurus Platform Patents, then Rhythm shall have the right, but shall not be obliged, at its own cost and expense to do so in accordance with the following, subject to the prior written consent of Camurus. If Camurus gives such consent, then the following procedures shall apply in these circumstances:

(i) Where Rhythm has requested and been granted approval by Camurus to commence proceedings in relation to any such Camurus Platform Patents not specifically claiming the Product (including any method of making or using the same), Rhythm shall be entitled to require Camurus to join Rhythm as co-plaintiff and Camurus shall have the right to join as co-plaintiff. In such case Camurus shall provide all necessary assistance to Rhythm in relation to any such proceeding and

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Rhythm shall on demand by Camurus pay or promptly reimburse Camurus for the costs of such activity unless Camurus elects to be separately represented (which shall be at Camurus' discretion), in which case such separate representation shall be at Camurus' cost and expense;

(ii) if Rhythm succeeds in any such infringement proceedings whether at trial or by way of settlement, the proceeds of any award or damages or settlement in respect of such infringement proceedings shall first be applied to reimburse (a) an amount equal to Rhythm' costs of taking the proceedings and (b) an amount equal to Camurus' costs referred in this Section 7.10, with the remainder being retained by Rhythm less []* per cent []* thereof, which amount shall be paid to Camurus;

(iii) Rhythm shall not enter into a settlement, consent judgment or other voluntary final disposition of an action or claim or counterclaim under this Section 7.10 without the prior written approval of Camurus, such consent not to be unreasonably withheld.

7.11

Hatch-Waxman Certifications. If either Party (i) reasonably believes that a Third Party may be filing or preparing or seeking to file a generic or abridged NDA that refers to or relies on regulatory documentation for a Product that was submitted by Rhythm to any Regulatory Authority, (ii) receives any notice of certification regarding any Patent Rights included in Camurus Patent Rights (i.e., Patent Rights Controlled by Camurus) or Rhythm Patent Rights (i.e., Patent Rights Controlled by Rhythm) pursuant to the Hatch-Waxman Act claiming that any such Patent Rights are invalid or unenforceable or claiming that the any such Patent Rights will not be infringed by the manufacture, use, marketing or sale of a product for which an ANDA is filed, or (iii) receives any equivalent or similar certification or notice in any other jurisdiction, it shall notify the other Party in writing, identifying the alleged applicant or potential applicant and furnishing the information upon which such determination is based, and provide the other Party a copy of any such notice of certification within five (5) days of receipt and the Parties' rights and obligations with respect to any legal action as a result of such certification shall be as set forth above in Sections 7.9 or 7.10.

8

CONFIDENTIALITY

8.1

Except to the extent expressly authorized by this Agreement including in Sections 8.3 and 8.4 or otherwise agreed in writing, each Recipient and its Affiliates and its Sublicensees and licensees in possession of Confidential Information of the Disclosing Party shall maintain such Confidential Information as confidential and use it only for the purposes of this Agreement in accordance with this Section 8. This obligation shall continue during the term of this Agreement and for a period equal to ten (10) years after the date of expiration or termination of this Agreement; provided, however, that this obligation shall continue to apply after such ten (10) year period to any Know-How, development data, other data, regulatory filings and other information disclosed, provided, licensed, transferred or otherwise made available by either Party to the other Party under this Agreement, until such time as such Know-How, development data, other data, regulatory filings and other information becomes exempt pursuant to subparagraphs (i) through (v) below. Each

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Party shall guard such Confidential Information using the same degree of care as it normally uses to guard its own confidential, proprietary information of like importance, but in any event no less than reasonable care. Notwithstanding the foregoing, the Recipient of the categories of Confidential Information identified in Sections 1.16 (i)-(iv) inclusive shall be relieved of the confidentiality and limited use obligations of this Agreement to the extent that the Recipient establishes by written evidence that:

- (i) the Confidential Information was previously known to the Recipient from sources other than the Disclosing Party at the time of disclosure and other than under an obligation of confidentiality and non-use;
- (ii) the Confidential Information was generally available to the public or otherwise part of the public domain at the time of its disclosure; or
- (iii) the Confidential Information became generally available to the public or otherwise part of the public domain after its disclosure to the Recipient Party other than through any act or omission of the Recipient Party in breach of this Agreement; or
- (iv) the Confidential Information is acquired in good faith in the future by the Recipient Party from a Third Party who has a lawful right to disclose such information and who is not under an obligation of confidence to the Disclosing Party with respect to such information; or
- (v) the Confidential Information is subsequently developed by or on behalf of the Recipient Party without use of the Disclosing Party's Confidential Information.

8.2 For clarity, specific aspects or details of Confidential Information shall not be deemed to be within the public domain or in the possession of the Recipient Party merely because the Confidential Information is embraced by more general information in the public domain or in the possession of the Recipient Party. Further, any combination of Confidential Information shall not be considered in the public domain or in the possession of the Recipient Party merely because individual elements of such Confidential Information are in the public domain or in the possession of the Recipient Party unless the combination is in the public domain or in the possession of the Recipient Party.

8.3 Notwithstanding the above obligations of confidentiality and non-use a Recipient may disclose Confidential Information:

(i) to a Regulatory Authority as reasonably necessary to obtain and maintain Regulatory Approval in a particular jurisdiction to the extent consistent with the licenses granted under terms of this Agreement, provided that reasonable effort will be taken to ensure confidential treatment of such information.

(ii) disclose Confidential Information: (a) to the extent such disclosure is reasonably necessary to comply with the order of a court; or (b) to the extent such disclosure is required to comply with a legal requirement, including to the extent such disclosure is required in publicly filed financial statements or other public statements or filings under rules governing a stock exchange or pursuant to

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applicable securities laws or regulations (e.g., the rules of the United States Securities and Exchange Commission, NASDAQ, NYSE, or any other stock exchange on which securities issued by either Party may be listed); provided, to the extent possible bearing in mind such legal requirements and subject to the next subsequent sentence of this Section 8.3.(ii), such Party shall provide the other Party with a copy of the proposed text of such statements or disclosure five (5) business days in advance of the date on which the disclosure is to be made to enable the other Party to review and provide comments, unless a shorter review time is agreed. If compliance with a legal requirement requires filing of this Agreement, the filing Party shall to the extent possible seek confidential treatment of portions of this Agreement from the relevant competent authority to the extent that such confidential treatment is available pursuant to applicable law and shall provide the other Party with a copy of the proposed filings at least five (5) business days prior to filing for the other Party to review any such proposed filing and provide comments. Each Party agrees that it will obtain its own legal advice with regard to its compliance with legal requirements and will not rely on any statements made by the other Party relating to such legal requirements; and

(iii) by filing or prosecuting Patent Rights, the filing or prosecution of which is contemplated by this Agreement, without violating Section 8.1; it being understood that publication of such filings occurs in some jurisdictions within eighteen (18) months of filing, and that such publication shall not violate the above secrecy provision.

(iv) to such Recipient's employees, Affiliates, contractors (including clinical researchers and CMO's), licensees, sublicensees, agents, consultants and potential business partners, as such Recipient reasonably determines is necessary to receive the benefit of the licenses and rights granted or available to it under this Agreement or to fulfill its obligations pursuant to this Agreement; provided, however, any such persons must be obligated to substantially the same extent as set forth in Section 8.1 to hold in confidence and not make use of such Confidential Information for any purpose other than those permitted by this Agreement and breach by such persons of their confidentiality obligations shall be deemed a breach by the Recipient of its confidentiality obligations hereunder. For the avoidance of doubt, it is understood and agreed that Camurus may not disclose any Confidential Information relating to the Product to any licensee of the FC Technology without the prior written consent of Rhythm except when exercising its rights under Sections 2.4 and 3.7.

(v) (a) to its actual or potential investment bankers; (b) to existing and potential investors in connection with an offering or placement of securities for purposes of obtaining financing for its business and to actual and prospective lenders for the purpose of obtaining financing for its business and to potential licensees or sublicensees of the FC Technology or any other rights licensed to the Recipient pursuant to this Agreement; and (c) to a bona fide potential acquirer or merger partner for the purposes of evaluating entering into a merger or acquisition, provided, however, any such persons must be obligated to substantially the same extent as set forth in Section 8.1 to hold in confidence and not make use of such Confidential Information for any purpose other than those permitted by this Agreement; and

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(vi) disclose Confidential Information to its legal advisers for the purpose of seeking advice.

8.4 Nothing in this Section 8 restricts either Party from using or disclosing any of its own Confidential Information for any purpose whatsoever; provided that, to the extent Know-How is exclusively licensed by one Party to the other, the licensor may not continue to use and disclose such Know-How in a manner not consistent with the exclusivity of the license granted.

8.5 Other than the press release pertaining to this transaction that the Parties have agreed upon and attached as Exhibit 8.5 to this Agreement and save as permitted in Section 8.3:

(i) neither Party, as a Recipient, shall make any public announcement or statement to the public containing Confidential Information of the Disclosing Party without the prior written consent of the Disclosing Party. No such public announcements or statements shall be made without the prior review and consent of the appropriate individual designated for the purpose by the other Party; and

(ii) save as may otherwise be provided herein neither Party shall mention or otherwise use the name or Trademark of the other Party or its Affiliates in any publication, press release, promotional material or other form of publicity without the prior written consent of the appropriate individual designated for the purpose by the other Party.

8.6 With respect to public disclosure required to be made pursuant to regulatory requirements or stock exchange rules applicable to a Party, each such Party will use reasonable efforts to submit to the other Party a draft of any public announcement (“Proposed Disclosure”) directly related to the Product at least three (3) business days prior to the date on which such Party plans to make such announcement, and in any event will submit such draft to the other Party at least twenty-four (24) hours prior to the release of such Proposed Disclosure. If a Party is unable to comply with the foregoing twenty-four (24)-hour notice requirement because of a legal obligation or stock or securities exchange requirement to make more rapid disclosure, such Party will not be in breach of this Agreement but will in that case give telephone and email notice to a senior executive of the other Party and provide a draft of the Proposed Disclosure with as much notice as possible prior to the release of such announcement. A Party that receives a draft of any Proposed Disclosure that the other Party is planning to make may not make any disclosure or public announcement of the substance or content of such Proposed Disclosure until such time as such other Party has released such Proposed Disclosure to the public. Any draft of any Proposed Disclosure provided by one Party to the other pursuant to this Section 8.6 shall be deemed and treated as Confidential Information of the Party that is proposing to make such Proposed Disclosure.

8.7 Notwithstanding the foregoing Camurus shall be entitled to include the name of Rhythm within a list of collaborators.

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9 REPRESENTATIONS AND WARRANTIES

9.1 Mutual Representations and Warranties of Camurus and Rhythm.

Each of Camurus and Rhythm hereby represents and warrants to the other Party as of the Effective Date as follows

- (a) It is duly organized, validly existing and in good standing under the laws of the jurisdiction of incorporation. It has the requisite legal and company power and authority to conduct its business as presently being conducted and as proposed to be conducted by it and is duly qualified to do business in those jurisdictions where its ownership of property or the conduct of its business requires
- (b) It has all requisite legal and company power and authority to enter into this Agreement and to grant the rights described herein. All company actions on its part, its boards of directors or managers, or similar governing body and its equity holders necessary for (i) the authorization, execution, delivery and performance by it of this Agreement, and (ii) the consummation of the transactions contemplated hereby, have been duly taken.
- (c) This Agreement is a legally valid and binding obligation of it, enforceable against it in accordance with its terms (except in all cases as such enforceability may be limited by applicable bankruptcy, insolvency, reorganization, moratorium, or similar laws affecting the enforcement of creditors' rights generally and except that the availability of the equitable remedy of specific performance or injunctive relief is subject to the discretion of the court or other tribunal before which any proceeding may be brought).
- (d) Each Party has and shall continue to have written contracts with all Third Parties (including employees and subcontractors) performing services on its behalf under this Agreement where such services are intended to create inventions that may be Collaboration Inventions that assign to such Party all Collaboration Inventions and rights therein.

9.2 Additional Representations and Warranties of Camurus.

Camurus hereby further represents and warrants to Rhythm as of the Effective Date that:

- (a) Save with respect to []* that have been disclosed in writing by Camurus to Rhythm prior to the Effective Date, Camurus is not aware of any pending actions, suits or other proceedings against it or any of its Affiliates that questions the validity of any issued Camurus Platform Patents, or that otherwise relate or pertain to, any Camurus Platform IP;
- (b) Camurus is not aware that any of the Camurus Platform Patents are invalid, and Camurus is not aware of any defect in Camurus' right, title and interest in and to the Camurus Platform Patents;

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- (c) To the extent necessary to grant Rhythm the rights provided for in this Agreement, Camurus owns or Controls sufficient rights in the Camurus Platform IP.
- (d) Camurus, to its knowledge and belief, has supplied Rhythm with all material documentation and information, possessed by Camurus or any of its Affiliates which have been requested by Rhythm []*, during the course of due diligence prior to execution of this Agreement.

- (e) Camurus is not aware of any use, infringement or misappropriation of the Camurus Platform IP in derogation of the rights granted to Rhythm in this Agreement. To the knowledge of Camurus, the practice and use of the Camurus Platform IP by Rhythm, its Affiliates or Sublicensees in the manner permitted or contemplated in this Agreement will not infringe upon, or constitute misappropriation or unauthorized use of, the Intellectual Property of any Third Party.
- (f) To the knowledge of Camurus, Camurus and its Affiliates have complied with all the requirements of all United States and foreign patent offices with respect to the filing of applications for Patent Rights in respect of the Camurus Platform Patents, including the duty of disclosure under 37 C.F.R. 1.56 and comparable provisions of foreign patent offices.
- (g) (i) To the knowledge of Camurus, Camurus and its Affiliates have complied with all the requirements of all United States and foreign patent offices to maintain the Camurus Platform Patents in full force and effect and (ii) to Camurus' knowledge, all necessary registration, maintenance and renewal fees have been paid and all necessary documents and certificates required to be filed in connection with the issued Camurus Platform Patents and pending applications for Patent Rights in respect of Camurus Platform Patents have been duly filed and the duty of disclosure under applicable patent laws have been fulfilled.
- (h) In each case in which Camurus or any of its Affiliates has acquired title to any inventions forming part of Camurus Platform Patents from any person, Camurus or any such Affiliate, as applicable, has obtained an assignment in form sufficient to transfer all rights in such inventions.
- (i) Exhibit 1.5 hereto lists all Patent Rights owned or Controlled by Camurus or any of its Affiliates on the Effective Date that cover the FC Technology. Except for the Patent Rights listed on Exhibit 1.5 hereto, neither Camurus nor any of its Affiliates owns or Controls any Patent Rights on the Effective Date pertaining to the FC Technology.
- (j) []*.

Notwithstanding anything to the contrary in this Agreement, a Party shall not be entitled to make any claims or bring any action against the other Party based on warranties or representations extended under this Agreement to the extent that the circumstances giving rise to such claim or action were known by or disclosed to the

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claiming Party prior to the Effective Date or could reasonably have been inferred from information disclosed by the other Party.

9.3

Disclaimer of Warranties.

EXCEPT AS OTHERWISE EXPRESSLY PROVIDED IN SECTION 9.1 AND SECTION 9.2 OF THIS AGREEMENT OR MANDATED BY APPLICABLE LAW (WITHOUT THE RIGHT TO WAIVE OR DISCLAIM), NEITHER PARTY MAKES ANY REPRESENTATION OR WARRANTY WITH RESPECT TO THE LICENSED COMPOUNDS, PRODUCTS, ANY TECHNOLOGY, GOODS, SERVICES, RIGHTS, OR OTHER SUBJECT MATTER OF THIS AGREEMENT AND HEREBY DISCLAIMS ALL WARRANTIES, CONDITIONS OR REPRESENTATIONS OF ANY KIND, EXPRESS OR IMPLIED, INCLUDING IMPLIED WARRANTIES OF PERFORMANCE, MERCHANTABILITY, SATISFACTORY QUALITY, FITNESS FOR A PARTICULAR PURPOSE OR NON-INFRINGEMENT OF THIRD PARTY INTELLECTUAL PROPERTY RIGHTS

10

INDEMNIFICATION

10.1

Indemnification by Rhythm. Subject to Sections 10.3, 10.4 and 10.5, Rhythm shall indemnify, defend and hold harmless Camurus, its Affiliates, and its and their respective, directors, officers, employees and agents (collectively, the "**Camurus Indemnified Party**") against any and all claims, liabilities, losses, damages, costs or expenses, including reasonable attorneys' fees, arising out of any claim or action brought by a Third Party (collectively, "**Losses**") incurred or suffered by the Camurus Indemnified Party to the extent arising out of or caused by:

- (i) the development, use, manufacture distribution, marketing, promotion or sale of Product by or on behalf of Rhythm or its Affiliates or Sublicensees in the Territory (including without limitation any claims based upon product liability and any claims arising from Camurus or its Affiliates provision of services under the Agreement); or
- (ii) the breach by Rhythm of one or more of its representations, warranties or other obligations under this Agreement;

provided, however, that Rhythm shall not be required to indemnify, hold harmless or defend any Camurus Indemnified Party against any claim brought pursuant to Section 10.2(i) or (ii) to the extent that Camurus has an obligation to indemnify the Rhythm Indemnified Parties under Section 10.2 (i) or (ii).

10.2

Indemnification by Camurus. Subject to Sections 10.3, 10.4 and 10.5, Camurus shall indemnify, defend and hold harmless Rhythm, its Affiliates, and its and their respective, directors, officers, employees and agents (collectively, the "**Rhythm Indemnified Party**") against any and all Losses (as defined above) incurred or suffered by the Rhythm Indemnified Party to the extent arising out of or caused by

- (i) the practice or use by Camurus or its Affiliates, licensees or sublicensees of the Rhythm Collaboration IP or the Joint IP; or

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(ii) the breach by Camurus of one or more of its representations, warranties or other obligations under this Agreement;

provided, however, that Camurus shall not be required to indemnify, hold harmless or defend any Rhythm Indemnified Party against any claim brought pursuant to Section 10.1(i) or (ii) to the extent that Rhythm has an obligation to indemnify the Camurus Indemnified Parties under Sections 10.1(i) or (ii).

10.3 **Notification of Liabilities/Losses.** In the event that either Party intends to seek indemnification for any claim under any of Sections 10.1 or 10.2, it shall inform the other Party of the claim promptly after receiving notice of the claim.

(i) In the case of a claim for which Camurus seeks indemnification under Section 10.1, Camurus shall permit Rhythm to direct and control the defence of the claim and shall provide such reasonable assistance as is reasonably requested by Rhythm (at Rhythm's cost) in the defence of the claim; provided that nothing in this Section 10.3 shall permit Rhythm to make any admission on behalf of Camurus, or to settle any claim or litigation which would impose any financial obligations on Camurus without the prior written consent of Camurus, such consent not to be unreasonably withheld or delayed.

(ii) In the case of a claim for which Rhythm seeks indemnification under Section 10.2, Rhythm shall permit Camurus to direct and control the defence of the claim and shall provide such reasonable assistance as is reasonably requested by Camurus (at Camurus' cost) in the defence of the claim, provided always that nothing in this Clause 10.3 shall permit Camurus to make any admission on behalf of Rhythm, or to settle any claim or litigation which would impose any financial obligations on Rhythm without the prior written consent of Rhythm, such consent not to be unreasonably withheld or delayed.

10.4 **Right to Participate in Defense.** Without limiting Section 10.3, any indemnitee will be entitled to participate in, but not control, the defense of a Third Party claim for which it has sought indemnification hereunder and to employ counsel of its choice for such purpose; provided, however, that such employment will be at the indemnitee's own expense unless (a) the employment and reimbursement thereof has been specifically authorized by the indemnifying Party in writing, or (b) the indemnifying Party has failed to assume the defense and employ counsel in accordance with section 10.3 (in which case the indemnified Party will control the defense).

10.5 **Cooperation.** If the indemnifying Party chooses to defend or prosecute any Third Party claim, the indemnified Party will, and will cause each other indemnitee to, cooperate in the defense or prosecution thereof and will furnish such records, information and testimony, provide such witnesses and attend such conferences, discovery proceedings, hearings, trials and appeals as may be reasonably requested in connection with such Third Party claim. Such cooperation will include access during normal business hours afforded to the indemnifying Party to, and reasonable retention by the indemnified Party of, records and information that are reasonably relevant to such Third Party claim, and making indemnities and other employees and agents available on a mutually convenient basis to provide additional

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information and explanation of any material provided hereunder, and the indemnifying Party will reimburse the indemnified Party for all of its reasonable out-of-pocket expenses incurred in connection with such cooperation.

10.6 **Reserved.**

10.7 **Exclusive Remedy.** Each Party agrees that its sole and exclusive remedy with respect to Losses shall be pursuant to the indemnification provisions of this Section 10.

10.8 **Insurance.** Immediately upon the first administration of a Product to a human in the Territory by Rhythm, its Affiliates or its permitted Sublicensees, and for a period of []* years after the expiration of this Agreement or the earlier termination thereof, Rhythm shall maintain Commercial General Liability Insurance and Product Liability Insurance, including contractual liability coverage, in an amount not less than []* per occurrence bodily injury/property damage combined and []* aggregate annually. Upon written request, the insuring Party shall provide the other Party with a certificate of insurance attesting to such coverage. It is understood and agreed that this insurance shall not be construed to limit either Party's liability with respect to its indemnification obligations hereunder.

11 TERM AND TERMINATION

11.1 **Term of Agreement.**

This Agreement shall become effective as of the Effective Date and, unless earlier terminated pursuant to other provisions of this Section 11, shall continue in full force and effect until the expiration of all Royalty Terms (the "Term"). On a country-by-country and Product-by-Product basis, after expiration of the Royalty Term for the Product in each country in the Territory, Rhythm shall have a royalty-free, non-exclusive license to develop, make, have made, use, import, market, promote, distribute, sell, and offer for sale and otherwise exploit such Product in such country.

11.2 Rhythm may terminate this Agreement without cause on a Product-by-Product basis or in its entirety at any time by giving not less than three (3) months prior written notice. Rhythm may terminate this Agreement on a Product-by-Product basis or in its entirety immediately following the withdrawal of Product from any market as a result of bona fide concerns based on specific and verifiable information that the applicable Product is unsafe for administration to humans (a "Valid Safety Issue"). For the avoidance of doubt, the ninety (90) day notice period applicable to termination under the first sentence of this Section 11.2 shall not apply in the case of termination for a Valid Safety Issue.

11.3 **Termination for Material Breach or Bankruptcy.**

- (a) Upon the material breach by one Party under this Agreement, the other Party shall notify the breaching Party of such breach, and require that the breaching Party cure such breach within sixty (60) days (or, in the case of payment defaults, within thirty (30) days).

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- (b) In the event that a material breach by Rhythm is not cured within the applicable cure period and without limiting other available remedies, Camurus shall have the right to terminate this Agreement upon written notice within thirty (30) days thereafter and all licenses granted by Camurus to Rhythm hereunder shall terminate, subject to the terms of Section 11.4.
- (c) In the event that a material breach by Camurus is not cured within the applicable cure period and without limiting other available remedies, Rhythm shall have the right to terminate this Agreement upon written notice within thirty (30) days thereafter, and, at Rhythm' option, all licenses granted by Camurus to Rhythm hereunder shall continue in full force and effect, subject to the continuing obligation to pay milestone payments, license fees, Royalties and sales milestones. Upon such termination by Rhythm for such Camurus material breach, (i) Camurus' obligations hereunder to provide Know-How and other materials and information to enable the use of such licenses shall continue; (ii) Camurus' right to use any Rhythm Development Data and Regulatory Approvals shall terminate, except in respect of rights which were previously granted by Camurus to a licensee in the Territory prior to date of such termination, and (iii) the following provisions shall also continue: Sections 2.1, 2.2, 2.3, 3.1, 3.5, 3.6, 3.8, 4, 5 and 7. Termination of this Agreement pursuant to this Section 11.3(c) will be without prejudice to any rights that will have accrued to the benefit of a Party prior to the effective date of such termination. Such termination will not relieve a Party from obligations that are expressly indicated to survive the termination of this Agreement.
- (d) Either Party may, without limiting other available remedies, terminate this Agreement, in whole by notice to the other Party in the event (i) the other Party shall have become bankrupt or shall have made an assignment for the benefit of its creditors; (ii) there shall have been appointed a trustee or receiver for the other Party or for all or a substantial part of its property; or (iii) any case or proceeding shall have been commenced or other action taken by or against the other Party in bankruptcy or seeking reorganization, liquidation, dissolution, winding-up, arrangement, composition or readjustment of its debts or any other relief under any bankruptcy, insolvency, reorganization or other similar act or law of any jurisdiction now or hereafter in effect, and any such event shall have continued for ninety (90) days undisputed, undismissed, unbonded and/or undischarged.
- (e) Rhythm may also terminate this Agreement in accordance with the provisions of Sections 3.6 and 5.2, and if Rhythm fails to deliver notice of termination or continuation to Camurus in accordance with the time periods specified in Sections 3.6 and 5.2 then Camurus may terminate this Agreement with immediate effect by giving written notice to Rhythm.
- (f) The Parties may terminate this Agreement, at any time upon mutual written agreement of the Parties.

- 11.4 Effect of Termination. Upon termination of this Agreement by either Party for any reason (other than termination by Rhythm pursuant to Section 11.3(c) or termination pursuant to Section 11.3(d)):

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- (a) Subject to Section 11.4(e) below, all licenses granted by Camurus to Rhythm shall terminate (including all rights to use any Camurus Platform IP);
- (b) all licenses and other rights granted Camurus to use any of the Rhythm Collaboration IP, Rhythm Development Data, Regulatory Approvals in the Territory shall continue, subject to all indemnity and other obligations of Camurus hereunder in respect thereof;
- (c) Rhythm shall discontinue Prosecution and abandon any Patent Rights claiming the Product.
- (d) Termination of this Agreement for any reason will be without prejudice to any rights that will have accrued to the benefit of a Party prior to the effective date of such termination. Such termination will not relieve a Party from obligations that are expressly indicated to survive the termination of this Agreement.
- (e) In the event this Agreement terminates for Rhythm's breach or bankruptcy, the license granted in Section 2.1 shall remain in force only to the extent required for each of Rhythm's Sublicensees at such time to continue to exercise its sublicensed rights provided, that, upon Camurus' written request, such Sublicensee agrees in writing with Camurus (within 30 days after such written request by Camurus) that Camurus is entitled to enforce all relevant obligations under the provisions of this Agreement directly against such Sublicensee and provided further, that Rhythm shall be jointly liable with such Sublicensee to Camurus for any action or inaction of the Sublicensees under this Agreement.
- (f) In case of termination without cause, neither party shall be liable to the other party for any compensation or damages by reason of such termination of this Agreement.

- 11.5 Termination for Patent Challenge. In the event that Rhythm or any of its Affiliates or Sublicensees commences or otherwise pursues, directly or indirectly (or voluntarily assists Third Parties to do so, other than as required by law or legal process), any proceeding seeking to have any of the Patent Rights forming part of Camurus Platform IP revoked or declared invalid, unpatentable, or unenforceable, Camurus may declare a material

breach hereunder that, if not cured within the thirty (30) days after Camurus gives written notice of such material breach to Rhythm and the applicable Affiliate or Sublicensee, shall give Camurus the right to terminate this Agreement with immediate effect .

- 11.6 **Surviving Provisions.** Except as otherwise provided in Section 11.3(c) and Section 11.4 above, in addition to the Sections that are expressly stated to survive termination, the following Sections of this Agreement shall survive any expiration or termination of this Agreement for any reason: Sections 1, 7.3(c), 7.3(e), 8, 9.3, 10, 11.4, 11.6 and 12.

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12 MISCELLANEOUS PROVISIONS

- 12.1 **Consequential Damages.** IN NO EVENT SHALL EITHER PARTY OR THEIR AFFILIATES BE LIABLE FOR SPECIAL, PUNITIVE, INDIRECT, INCIDENTAL OR CONSEQUENTIAL DAMAGES AS WELL AS LOST PROFITS, WHETHER BASED ON CONTRACT, TORT OR ANY OTHER LEGAL THEORY AND IRRESPECTIVE OF WHETHER SUCH PARTY HAS BEEN ADVISED OF THE POSSIBILITY OF ANY SUCH LOSS OR DAMAGE; PROVIDED, THAT THIS LIMITATION SHALL NOT LIMIT THE INDEMNIFICATION OBLIGATION OF SUCH PARTY UNDER THE PROVISIONS OF SECTION 10 FOR SUCH DAMAGES CLAIMED BY A THIRD PARTY AND NOTHING IN THIS SECTION 12.1 IS INTENDED TO LIMIT RHYTHM'S PAYMENT OBLIGATIONS UNDER SECTION 5 OR EITHER PARTY'S OBLIGATIONS UNDER SECTION 7 OR SECTION 8.
- 12.2 **Assignment.** Neither Party shall have the right to assign this Agreement, nor any of its rights hereunder, nor delegate any of its obligations hereunder, without the prior written consent of the other Party, which shall not be unreasonably withheld or delayed. Notwithstanding the foregoing, (i) Camurus and Rhythm may assign this Agreement to any purchaser of all or substantially all of its assets or to any successor entity resulting from any merger or consolidation of Camurus or Rhythm with or into such entity, or (ii) Camurus and Rhythm may assign this Agreement to any of its Affiliates but only for as long as such Affiliate remains an Affiliate of the assigning Party provided that such Affiliate agrees to be bound hereunder. Any attempt to assign this Agreement in breach of the foregoing shall be void. This Agreement shall be binding upon and inure to the benefit of the Parties hereto and each of their successors and permitted assigns.
- 12.3 **Further Actions.** Each Party agrees to execute, acknowledge and deliver such further instruments, and to do all such other acts, as may be necessary or appropriate in order to carry out the purposes and intent of this Agreement.
- 12.4 **Compliance with Laws.** Each Party shall review in good faith and cooperate in taking actions to ensure compliance of this Agreement and the Parties' activities hereunder with all applicable laws, rules, ordinances, regulations and guidelines. Each Party shall provide the other Party such reasonable assistance as may be required for the Party requesting such assistance to comply with all such laws, rules, ordinances, regulations and guidelines of all governmental entities, bureaus, and agencies having jurisdiction pertaining to this Agreement, including obtaining all import, export and other permits, certificates, licenses or the like required by such laws, rules, ordinances, regulations and guidelines necessary to permit the Parties to perform hereunder and to exercise their respective rights hereunder.
- 12.5 **Force Majeure.** Neither Party shall be responsible or liable in any way for failure or delay in carrying out the terms of this Agreement (other than any payment or confidentiality obligations) resulting from fire, flood, other natural disasters, war, labor difficulties, interruption of transit, accident, explosion, civil commotion, and acts of any governmental authority; provided, that the Party so affected shall give prompt notice thereof to the other. If any such cause prevents either Party from performing any of its material obligations hereunder for more than ninety (90) days,

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the other Party may then terminate this Agreement upon thirty (30) days prior notice. Except as provided in the preceding sentence, no such failure or delay shall terminate this Agreement, and each Party shall complete its obligations hereunder as promptly as reasonably practicable following cessation of the cause or circumstances of such failure or delay

- 12.6 **Notices.** All notices and other communications hereunder shall be in writing and shall be deemed given when delivered personally or by facsimile transmission (receipt verified), five (5) days after mailed by registered or certified air mail (return receipt requested), postage prepaid, or two (2) days after sent by express courier service, to the Parties at the following addresses (or at such other address for a Party as shall be specified by like notice; provided, that notices of a change of address shall be effective only upon receipt thereof):

If to Camurus, addressed to:

Camurus AB
att: CEO
Ideon Science Park
Sölvegatan 41
SE_223 70 Lund
Sweden
Phone: +46 46286 5730
Fax: +46 46 286 5739

If to Rhythm, addressed to:

Rhythm Pharmaceuticals, Inc.
855 Boylston Street, 11th Floor
Boston, MA 02116 USA
Attn: Chief Executive Officer
Phone: 857 264 4280
Fax: 857 264 4299

- 12.7 **Amendment.** No amendment, modification or supplement of any provision of this Agreement shall be valid or effective unless made in a writing that explicitly refers to this Agreement and that is signed by a duly authorized officer of each Party.
- 12.8 **Waiver.** Except to the extent otherwise expressly set forth in this Agreement, the rights and remedies of the Parties set forth herein or otherwise available at law or equity are cumulative and not alternative. No provision of this Agreement shall be waived by any act, omission or knowledge of any Party or its agents or employees except by an instrument in writing expressly waiving such provision and signed by a duly authorized officer of the waiving Party.
- 12.9 **Counterparts.** This Agreement shall be executed in two or more counterparts, each of which shall contain the signature of the Parties and all such counterparts shall

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constitute one and the same agreement. Counterparts may be delivered via facsimile, electronic mail (including pdf) or other transmission method and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for all purposes.

- 12.10 **Descriptive Headings.** The descriptive headings of this Agreement are for convenience only, and shall be of no force or effect in construing or interpreting any of the provisions of this Agreement.
- 12.11 **Severability.** Whenever possible, each provision of this Agreement shall be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Agreement is held to be prohibited by or invalid under applicable law, such provision shall be ineffective only to the extent of such prohibition or invalidity, without invalidating the remainder of this Agreement and the Parties shall in good faith seek to agree on an alternative provision reflecting the intent of the Parties that is enforceable.
- 12.12 **Entire Agreement.** This Agreement shall constitute and contain the complete, final and exclusive understanding and agreement of the Parties and cancels and supersedes any and all prior negotiations, correspondence, understandings and agreements, whether oral or written, between the Parties with respect to the subject matter hereof. The Confidentiality Agreement previously entered into between the Parties shall terminate as of the Effective Date and the Parties rights and obligations in respect of the Confidential Information disclosed under the Confidentiality Agreement shall thereafter be governed by this Agreement.
- 12.13 **Governing Law.** Except to the extent otherwise expressly provided elsewhere in this Agreement, this Agreement and all disputes arising out of it (including non-contractual disputes) shall be governed by and interpreted in accordance with the substantive laws of England, without regard to the choice of law provisions thereof. The United Nations Convention on Contracts for the International Sale of Goods shall not apply to the transactions contemplated by this Agreement.
- 12.14 **Dispute Resolution.**
- (a) The Parties recognize that a bona fide dispute as to certain matters may from time to time arise during the Term of this Agreement that relate to any Party's rights or obligations hereunder. In the event of the occurrence of any dispute arising out of or relating to this Agreement, including any question regarding its existence, validity or termination, either Party may, by written notice to the other, have such dispute referred to its respective officer designated below or their successors, for attempted resolution by good faith negotiations within sixty (60) days after such notice is received. If either Party desires to pursue arbitration under paragraph (b) below to resolve any such dispute, a referral to such executives under this paragraph (a) shall be a mandatory condition precedent. Said designated officers are as follows.

For Camurus: Chief Executive Officer

For Rhythm: Chief Executive Officer

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- (b) In the event that they shall be unable to resolve the dispute by executive mediation within such sixty (60) day period and do not mutually agree to extend the time for negotiation, then subject to Section 3.4 and Section 7.2(b), the dispute shall be submitted to and finally settled by binding arbitration in accordance with the procedure set forth in Sections 12.14(c)-(d).

- (c) Except with respect to actions by either Party seeking equitable or declaratory relief as described in Section 12.14(e), any claim or controversy arising in whole or in part under or in connection with this Agreement or the subject matter hereof that is not resolved pursuant to Section 12.14(b) or Section 3.4 or Section 7.2, as applicable, will be referred to and finally resolved by arbitration in accordance with the Rules of the International Chamber of Commerce (the “Rules”) as such Rules may be modified by this Agreement, by one arbitrator, who will be agreed upon by the Parties. If the Parties are unable to agree upon a single arbitrator within thirty (30) days following the date arbitration is demanded, three arbitrators will be used, one selected by each Party within ten (10) days after the conclusion of the 30-day period and a third selected by the first two within ten (10) days thereafter. The arbitrator(s) will resolve any discovery disputes. Either Party may commence arbitration proceedings by notice to the other Party. The Arbitration Institute of International Chamber of Commerce shall administer any arbitration proceeding. The place of arbitration shall be London, England. The arbitration shall be conducted in English. The award of arbitration shall be final and binding upon both Parties.
- (d) Except to the extent otherwise expressly provided in this Agreement, the arbitrator(s) will apply the laws of England. Judgment on the award granted in any arbitration hereunder may be entered in any court having jurisdiction over the award or any of the Parties or any of their respective assets. The Parties knowingly and voluntarily waive their rights to have their dispute tried and adjudicated by a judge and jury except as expressly provided herein.
- (e) Nothing in this Section 12.14 will prevent a Party from resorting to judicial proceedings if: (i) interim relief from a court is necessary to prevent serious and irreparable injury to such Party; or (ii) litigation is required to be filed prior to the running of the applicable statute of limitations. The use of any alternative dispute resolution procedure will not be construed under the doctrine of laches, waiver or estoppel to affect adversely the rights of either Party. Despite such action the Parties shall continue to participate in good faith in the procedures specified in this Section 12.14.

12.15 Independent Contractors. Nothing herein shall be construed to create any relationship of employer and employee, agent and principal, partnership or joint venture between the Parties. Each Party is an independent contractor. Neither Party shall have authority to make any statements, representations, or commitments of any kind, or to take any action which shall be binding on the other Party, except as may be explicitly provided for herein or otherwise authorized in writing.

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This Agreement has been executed in two (2) original copies of which the (Parties) have taken one (1) each. The Agreement shall come into force on the date given at the beginning of this Agreement.

For and on behalf of Camurus AB

Date: January 4, 2016

Signed by: /s/ Fredrik Tiberg

Full name: Fredrik Tiberg

Position: President & CEO

For and on behalf of Rhythm Pharmaceuticals, Inc.

Date: January 4, 2016

Signed by : /s/ Bart Henderson

Full name: Bart Henderson

Position: President

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EXHIBIT 1.5
CAMURUS PLATFORM IP PATENT RIGHTS

Short title (ref no.)	Filed in (main jurisdictions)	Granted in	Patent #
[]*			

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EXHIBIT 1.7
CAMURUS TRADEMARKS

Trademarks	Country	Classes	Registration number
[]*			

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EXHIBIT 1.19
DEVELOPMENT PLAN

See Attachment

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* CONFIDENTIAL TREATMENT REQUESTED. OMITTED PORTIONS FILED WITH THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO RULE 406 PROMULGATED UNDER THE SECURITIES ACT OF 1933, AS AMENDED

EXHIBIT 7.2 (c)
EXPERT'S DETERMINATION

1. Any matter or dispute to be determined by an expert under Section 7.2(c) of this Agreement ("Expert") shall be referred to a person suitably qualified to determine that particular matter or dispute who shall be nominated jointly by the Parties or, failing agreement between the Parties within twenty (20) Business Days of a written request by either Party to the other seeking to initiate the Expert's decision procedure, either party may request the President for the time being of the Association of the British Pharmaceutical Industry or any successor body to it to nominate the Expert.
2. The Parties shall, within fourteen (14) days of the appointment of the Expert, meet with him/her in order to agree a program for oral and written submissions.
3. In all cases the terms of appointment of the Expert by whomsoever appointed shall include:
 - 3.1 a commitment by the Parties to share equally the Expert's fee;
 - 3.2 a requirement on the Expert to act fairly as between the Parties and according to the principles of natural justice;
 - 3.3 intentionally omitted;
 - 3.4 a commitment by the Parties to supply to the Expert the submissions the subject of paragraph 2 and all such assistance, documents and information as he/she may require for the purpose of his or her determination.
 - 3.5 a commitment by the Parties that all negotiations connected with the dispute shall be conducted in confidence and without prejudice to the rights of the parties in any future proceedings.

4. The Expert shall, within forty-five (45) days of his/her appointment, give a written decision which shall contain a factual analysis, his/her conclusions and the reasons for his/her conclusions.
5. The Expert's decision shall be final and binding on the Parties (save in the case of manifest error).
6. The Parties expressly acknowledge and agree that they do not intend the reference to the Expert to constitute an arbitration within the scope of any arbitration legislation, the Expert's decision is not a quasi judicial procedure and the Parties shall have no right of appeal against the Expert's decision except as provided in Paragraph 5.

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**EXHIBIT 8.5
PRESS RELEASE**

13 Rhythm and Camurus Announce License Agreement for Extended Release FluidCrystal Setmelanotide

BOSTON and LUND, Sweden, January 5, 2016—Rhythm and Camurus announced today a license agreement for the use of Camurus' drug delivery technology, FluidCrystal®, to formulate setmelanotide (RM-493), Rhythm's novel melanocortin-4 receptor (MC4R) agonist. Under the terms of the agreement, Camurus has granted Rhythm a worldwide license to the FluidCrystal technology to formulate setmelanotide and to develop, manufacture, and commercialize this new formulation that has the potential for once-weekly dosing, administered as a subcutaneous injection. Rhythm plans to initiate a Phase I clinical trial with the setmelanotide FluidCrystal formulation after completing GMP manufacturing.

"We have developed a setmelanotide formulation with Camurus with an impressive sustained-duration profile," said Bart Henderson, President of Rhythm. "We believe this new formulation will provide a significant benefit to patients, improving compliance and ease of use with once-weekly dosing."

"The partnership with Rhythm follows the formulation development and preclinical assessment of this compelling drug candidate based on our FluidCrystal Injection depot technology," said Fredrik Tiberg, President and CEO of Camurus. "Rhythm's setmelanotide represents a novel approach to treating patients suffering from life-threatening obesity due to these rare and serious genetic disorders."

The license granted to Rhythm is specific to the FluidCrystal technology incorporating setmelanotide. The formulation has been developed in a collaboration between the companies. Under the terms of the license agreement, Rhythm is responsible for manufacturing, development, and commercialization of the setmelanotide FluidCrystal formulation worldwide. Camurus is eligible to receive an upfront payment and progressive payments of approximately \$65 million, of which the majority are sales milestones. In addition, Camurus is eligible to receive tiered, mid to mid-high, single digit royalties on future sales of the product.

About Setmelanotide (RM-493)

Setmelanotide is a potent, first-in-class MC4R agonist in development for the treatment of obesity caused by genetic deficiencies in the MC4 pathway, a key pathway in humans that regulates energy expenditure, homeostasis, and appetite. The critical role of the MC4 pathway in weight regulation was validated with the discovery that single genetic defects along this pathway result in early-onset and severe obesity. A Phase 2 setmelanotide trial is ongoing for the treatment of Prader-Willi syndrome (PWS), a rare genetic disorder that causes life-threatening obesity. Recent scientific evidence implicates defects in the MC4 pathway as the likely cause of the weight and appetite abnormalities in PWS. A second Phase 2 trial is ongoing for the treatment of pro-opiomelanocortin (POMC) deficiency obesity, a very rare, life-threatening genetic disorder of the MC4 pathway associated with unrelenting appetite and obesity.

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About FluidCrystal Injection Depot

The FluidCrystal Injection depot delivers therapeutic levels of drug substance over extended periods—tunable from days to months—from a single injection. While traditional depot therapeutics comprise complicated microsphere technology, Camurus' depot offers a liquid solution that transforms into a controlled release liquid crystal gel matrix in situ on contact with minute quantities of aqueous fluid at site of injection. The FluidCrystal delivery system overcomes traditional side effects associated with high initial drug release on injection (drug burst) and poor drug stability by effectively encapsulating the drug compound in the nanopores of the depot matrix throughout the entire process from injection until final degradation. This, together with the ready-to-use product design, makes the system highly suitable for sustained parenteral delivery of peptides and proteins. FluidCrystal is a registered trademark of Camurus AB.

About Rhythm (www.rhythmtx.com)

Rhythm is a biopharmaceutical company focused on developing peptide therapeutics for the treatment of rare genetic deficiencies that result in life-threatening metabolic disorders. Rhythm's lead peptide product candidate is setmelanotide, a first-in-class melanocortin 4 receptor (MC4R) agonist for the treatment of rare genetic disorders of obesity. The company is based in Boston, Massachusetts.

About Camurus

Camurus is a Swedish research-based pharmaceutical company committed to developing and commercializing innovative and differentiated medicines for the treatment of severe and chronic conditions. New drug products with best-in-class potential are conceived based on the proprietary FluidCrystal® drug delivery technologies and an extensive R&D expertise. Camurus' clinical pipeline includes products for treatment of cancer, endocrine diseases, pain, and addiction, developed in-house and in collaboration with international pharmaceutical companies. The company's share is listed on Nasdaq Stockholm under the ticker "CAMX." For more information, visit www.camurus.com.

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RHYTHM PHARMACEUTICALS, INC.**2017 EMPLOYEE STOCK PURCHASE PLAN****RHYTHM PHARMACEUTICALS, INC.****2017 EMPLOYEE STOCK PURCHASE PLAN****1. Purpose and History**

The purpose of this Plan is to give Employees wishing to do so a convenient means of purchasing Common Stock of the Company through payroll deductions. The Company believes that ownership of Common Stock by Employees will foster greater Employee interest in the Company's growth and development.

This Plan was adopted by the Board on September 22, 2017. It is the Company's intention that the Plan qualify as an "employee stock purchase plan" under Section 423 of the Code. The provisions of the Plan shall, accordingly, be construed in a manner consistent with the requirements of that Code section.

2. Definitions

As used in this Plan, the following terms shall have the following meanings:

2.1. Board means the Company's Board of Directors.

2.2. Business Day means a day on which the NASDAQ Stock Market (or any other national securities exchange on which the Common Stock is then listed) is open for trading. Every date under this Plan that falls on a weekend, a holiday or any other day that is not a Business Day (and any event that occurs after 5 p.m. eastern time on any date) shall be deemed automatically to fall on the next Business Day.

2.3. Code means the Internal Revenue Code of 1986, as amended from time to time, or any successor statute thereto, and any regulations issued from time to time thereunder.

2.4. Commission means the U.S. Securities and Exchange Commission.

2.5. Committee means the Compensation Committee of the Board or such other committee delegated responsibility by the Board for the administration of the Plan, as provided in Section 4 of the Plan. For any period during which no such committee is in existence "Committee" shall mean the Board and all authority and responsibility assigned to the Committee under the Plan shall be exercised, if at all, by the Board.

2.6. Common Stock or Stock means the common stock, par value \$0.001 per share, of the Company.

2.7. Company means Rhythm Pharmaceuticals, Inc., a corporation organized under the laws of the State of Delaware.

2.8. Compensation means an Employee's total compensation, including base pay or regular earnings plus commissions, bonuses, and overtime.

2.9. Continuous Status as an Employee means the absence of any interruption or termination of service as an Employee. Continuous Status as an Employee shall not be considered interrupted in the case of (i) sick leave; (ii) military leave; (iii) any other leave of

absence approved by the Plan administrator, provided that such leave is for a period of not more than three months, unless reemployment upon the expiration of such leave is guaranteed by contract or statute, or unless provided otherwise pursuant to Company policy adopted from time to time; or (iv) transfers between locations of the Company or between the Company and a Covered Entity.

2.10. Contributions means all amounts credited to the account of a Participating Employee pursuant to the Plan.

2.11. Corporate Transaction means any (1) merger or consolidation of the Company with or into another entity as a result of which the Stock of the Company is converted into or exchanged for the right to receive cash, securities or other property or is cancelled, (2) sale or exchange of Stock of the Company possessing more than fifty percent (50%) of the total combined voting power of the Company's outstanding securities for cash, securities or other property, (3) sale, transfer, or other disposition of all or substantially all of the Company's assets to one or more other persons in a single transaction or series of related transactions or (4) liquidation or dissolution of the Company; except, in the case of clauses (1) and (2), for a transaction the principal purpose of which is to change the state in which the Company is incorporated.

2.12. Covered Entity means any Subsidiary (whether now existing or subsequently established or acquired) that may adopt the Plan from time to time in accordance with the procedures set forth in Section 14 hereof with the Company's consent.

2.13. Effective Date means the IPO Date.

2.14. Employee means an employee of the Company or a Covered Entity who is customarily employed for at least 20 hours per week and more than five months in a calendar year. The Committee may, prior to the start of the applicable Plan Period, waive one or both of the twenty (20) hour and five

(5) month service requirements and/or establish such other eligibility requirements as it deems appropriate.

- 2.15. Exchange Act means the Securities Exchange Act of 1934, as amended.
- 2.16. Fair Market Value has the meaning set forth in Section 6.4(c).
- 2.17. Initial Plan Period means the first Plan Period of the Plan.
- 2.18. IPO Date means the date of the closing of the initial public offering of shares of Common Stock.
- 2.19. New Plan Period Termination Date has the meaning set forth in Section 12.4.
- 2.20. Participating Employee means an Employee who elects to participate in the Plan pursuant to Section 6.2(b).
- 2.21. Plan means this Rhythm Pharmaceuticals, Inc. 2017 Employee Stock Purchase Plan.
- 2.22. Plan Period Commencement Date means the first business day of each Plan Period.

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- 2.23. Plan Period Termination Date means the last business day of each Plan Period.

2.24. Plan Period means each successive period described in Section 6.1, at the end of which each Participating Employee (whose participation has not terminated pursuant to Section 6.7) shall purchase Shares.

- 2.25. Securities Act means the Securities Act of 1933, as amended.

2.26. Purchase Price means with respect to a Plan Period an amount equal to or greater than eighty five percent (85%) of the Fair Market Value of a Share on the Plan Period Commencement Date or on the Plan Period Termination Date, whichever is lower.

- 2.27. Share means a share of Common Stock, as adjusted in accordance with Section 12 of the Plan.

2.28. Subsidiary means a corporation, in an unbroken chain of corporations beginning with the Company if, at the time of the granting of the option, each of the corporations other than the last corporation in the unbroken chain owns stock possessing fifty percent (50%) or more of the total combined voting power of all classes of stock in one of the other corporations in such chain.

3. Shares Reserved For The Plan

Subject to adjustment as provided in Section 12 hereof, the number of Shares reserved for issuance hereunder shall be [258,433](1), provided, however, that the number of Shares authorized under this Section 3 of the Plan will be increased each January 1, commencing on January 1 of the year following the year in which the IPO Date occurs and ending on (and including) January 1, 2027, by an amount equal to the lesser of (i) one percent (1.0%) of outstanding Shares as of the end of the immediately preceding fiscal year and (ii) [646,083].(2) Notwithstanding the foregoing, the Board may act prior to January 1 of a given year to provide that there will be no such January 1 increase in the number of Shares authorized under this Section 3 of the Plan for such year or that the increase in the number of Shares authorized under this Section 3 of the Plan for such year will be a lesser number than would otherwise occur pursuant to the preceding sentence. For purposes of applying the foregoing limitation, if any option expires, terminates or is cancelled for any reason without having been exercised in full, the Shares not purchased or received by the Employee shall again be available for options to be granted under the Plan. Shares issued pursuant to the Plan may be either authorized but unissued shares or shares held by the Company in its treasury.

4. Administration

The Plan shall be administered by the Committee, *provided, however,* that at any time and on any one or more occasions the Board may itself exercise any of the powers and responsibilities assigned to the Committee under the Plan and when so acting shall have the benefit of all of the provisions of the Plan pertaining to the Committee's exercise of its authority

(1) To equal 1.0% of outstanding common stock on the Effective Date.

(2) Insert number equal to 2.5% of outstanding common stock post-IPO.

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hereunder; and *provided, further,* that the Committee may delegate its duties in order to facilitate the purchase and transfer of Shares and to provide for the day-to-day administration of the Plan with all powers necessary to enable the delegate to carry out its duties in that respect. Subject to the provisions of the Plan, the Committee shall have complete authority, in its discretion, to make or to select the manner of making all determinations with respect to each option to be granted by the Company under the Plan. In making such determinations, the Committee may take into account such factors as the Committee in its discretion shall deem relevant. Subject to the provisions of the Plan, the Committee shall also have complete authority to interpret the Plan, to prescribe, amend and rescind rules and regulations relating to it and to make all other determinations necessary or advisable for the administration of the Plan. The Committee's determinations made in good faith on matters referred to in the Plan shall be final, binding and conclusive on all persons having or claiming any interest under the Plan or an option granted pursuant hereto.

5. Eligibility for Awards

Subject to the requirements of Section 6.2 and the limitations imposed by Section 423(b) of the Code, any Employee shall be eligible to participate in a Plan Period under the Plan as of the applicable Plan Period Commencement Date. Notwithstanding any provision of the Plan to the contrary, no Employee shall be granted an option under the Plan (i) if, immediately after the grant, such Employee (taking into account stock which would be attributed to such Employee pursuant to Section 424(d) of the Code) would own capital stock of the Company and/or hold outstanding options to purchase stock possessing five percent (5%) or more of the total combined voting power or value of all classes of stock of the Company or of any Subsidiary of the Company, or (ii) if such option would permit his or her rights to purchase stock under all employee stock purchase plans (described in Section 423 of the Code) of the Company and its Subsidiaries to accrue at a rate which exceeds twenty-five thousand dollars (\$25,000) of such stock (determined on the basis of the Fair Market Value of such stock on the date or dates such option was granted) for each calendar year in which such option is outstanding at any time.

6. Terms of Participation

6.1. Plan Periods. The Initial Plan Period shall commence on May 1 or November 1 of such calendar year as the Committee may determine in its sole discretion and continue for six months. After the Initial Plan Period, there will be two consecutive six-month Plan Periods during each twelve month period thereafter, with the first six-month Plan Period beginning on May 1 and ending on the immediately following October 31, and the second six-month Plan Period beginning on November 1 and ending on the immediately following April 30 unless otherwise determined by the Committee.

6.2. Election to Participate and Plan Deductions.

(a) Shares shall be offered for purchase under the Plan through a series of successive, non-overlapping Plan Periods until such time as (i) the maximum number of Shares available for issuance under the Plan shall have been purchased or (ii) the Plan shall have been sooner terminated. At any time and from time to time, the Committee may change the duration and/or the frequency of Plan Periods or suspend operation of the Plan with respect to Plan Periods not yet commenced.

(b) An eligible Employee may become a Participating Employee in the Plan

by completing an enrollment agreement provided by the Company and filing it with the Company at least three business days prior to the Plan Period Commencement Date for the Plan Period in which such Employee desires to participate, unless either an earlier or later time for filing the enrollment agreement is set by the Committee for all eligible Employees with respect to a given Plan Period. The enrollment agreement shall set forth the percentage of the Employee's Compensation (subject to Section 6.2(c) below) to be paid as Contributions pursuant to the Plan. Payroll deductions shall commence on the first payroll following the Plan Period Commencement Date and shall end on the last payroll paid on or prior to the Plan Period Termination Date, unless sooner terminated by the Participating Employee as provided in Section 6.7.

(c) A Participating Employee may elect to have payroll deductions taken from each payroll during any Plan Period in an amount, in whole percentages, not less than one percent (1%) and not more than fifteen percent (15%) (or such other percentage as the Committee may establish from time to time before any Plan Period Commencement Date) of such Participating Employee's Compensation on each payroll date during the Plan Period. All payroll deductions made by a Participating Employee shall be credited to his or her account under the Plan. No interest shall accrue on Contributions to the Plan. A Participating Employee may not make any additional payments into such account.

(d) Unless the Committee announces otherwise before the start of a particular Plan Period, an eligible Employee's enrollment agreement in effect at the end of one Plan Period will remain in effect for each subsequent Plan Period.

(e) A Participating Employee may discontinue his or her participation in the Plan as provided in Section 6.7. A Participating Employee may, at any time during the Plan Period, reduce the rate of his or her payroll deduction to become effective as soon as administratively possible after filing the appropriate form with the Committee. The Participating Employee may not, however, effect more than one (1) such reduction per Plan Period. A Participating Employee may choose to increase his or her payroll deductions at any time during the specified enrollment period communicated to employees prior to the start of a Plan Period to be effective with that Plan Period.

(f) Notwithstanding the foregoing, to the extent necessary to comply with Section 423(b)(8) of the Code and Section 5 hereof, a Participating Employee's payroll deductions may be decreased during any Plan Period to zero percent (0%). Payroll deductions reduced to zero percent (0%) in compliance with this Section 6.2(f) shall re-commence automatically at the rate provided in such Participating Employee's enrollment agreement at the beginning of the next Plan Period, unless terminated by the Participating Employee as provided in Section 6.7.

(g) Any amounts left over in a Participating Employee's account upon expiration or termination of the Plan (or upon a withdrawal by a Participating Employee or upon a Participating Employee purchasing the maximum dollar amount or number of shares hereunder) shall be returned to the Participating Employee.

6.3. Shares.

(a) If the Committee determines that, on a given Plan Period Termination Date, the number of shares with respect to which options are to be exercised may exceed (i) the number of Shares that were available for sale under the Plan on the Plan Period Commencement

Date, or (ii) the number of shares available for sale under the Plan on such Plan Period Termination Date, then the Company shall make a pro rata allocation of the Shares available for purchase on such Plan Period Termination Date in as uniform a manner as shall be practicable and as it shall determine in its sole discretion to be equitable among all Participating Employees exercising options to purchase Common Stock on such Plan Period Termination Date. The Company shall make a pro rata allocation of the Shares available on the Plan Period Commencement Date pursuant to the preceding sentence, notwithstanding any authorization of additional Shares for issuance under the Plan by the Company's stockholders subsequent to such Plan Period Commencement Date.

(b) The Participating Employee shall have no interest or voting right in Shares covered by his or her option until such option has been exercised.

(c) Shares to be delivered to a Participating Employee under the Plan will be registered in the name of the Participating Employee.

6.4. Grant of Options.

(a) A Participating Employee shall be granted a separate option for each Plan Period in which he or she participates. The option shall be granted on the Plan Period Commencement Date for the Plan Period and shall provide the Participating Employee with the right to purchase Shares upon the terms set forth below.

(b) The number of Shares purchasable by a Participating Employee on each Plan Period Termination Date during the Plan Period, pursuant to Section 6.5 below, shall be determined by dividing such Employee's Contributions accumulated during such Plan Period up to such Plan Period Termination Date and credited to the Participating Employee's account as of the Plan Period Termination Date by the applicable Purchase Price. However, the maximum number of Shares a Participating Employee may purchase during each Plan Period shall not exceed 3,000 Shares, or such other number as may be determined by the Committee and announced to Employees at least five days prior to the scheduled beginning of the next Plan Period to be affected by the Committee's determination, provided that such purchase shall be subject to the limitations set forth in Section 6.2(c).

(c) The fair market value of the Shares on a given date (the "Fair Market Value") means the value of a share of Common Stock on a particular date determined by such methods or procedures as may be established by the Committee. Unless otherwise determined by the Committee, the Fair Market Value of the Common Stock as of any date, is (a) the closing price for the Common Stock as reported by the NASDAQ Stock Market (or on any other national securities exchange on which the Common Stock is then listed) for that date or, if no closing price is reported for that date, the closing price on the next preceding date for which a closing price was reported or (b) if the Common Stock is not traded on a national securities exchange but is traded over-the-counter, the closing or last price of the Common Stock on the composite tape or other comparable reporting system on that date or, if such date is not a trading day, the last market trading day prior to such date.

6.5. Exercise. Unless a Participating Employee withdraws from the Plan as provided

in Section 6.7, each option shall be exercised automatically on each Plan Period Termination Date, and Shares shall accordingly be purchased on behalf of each Participating Employee on each such Plan Period Termination Date. The purchase shall be effected by applying the Participating Employee's payroll deductions for the Plan Period ending on such Plan Period Termination Date to the purchase of Shares (subject to the limitation on the maximum number of Shares purchasable per Participating Employee on any one Plan Period Termination Date) at the Purchase Price in effect for the Participating Employee for that Plan Period Termination Date. The Shares purchased upon exercise of an option hereunder shall be deemed to be transferred to the Participating Employee on the Plan Period Termination Date. During his or her lifetime, a Participating Employee's option to purchase Shares hereunder is exercisable only by him or her.

6.6. Delivery. As promptly as practicable after each Plan Period Termination Date, the Company shall arrange for the delivery to each Participating Employee of a certificate or certificates or book-entry authorization and instruction to the Company's transfer agent and registrar for the number of Shares purchased upon exercise of his or her option.

6.7. Voluntary Withdrawal; Termination of Employment.

(a) A Participating Employee may withdraw all but not less than all of the Contributions credited to his or her account under the Plan up to two weeks prior to the Plan Period Termination Date by giving written notice to the Company in accordance with the Company's policy regarding withdrawal from the Plan. All of the Participating Employee's Contributions credited to his or her account will be paid to him or her promptly after receipt of his or her notice of withdrawal and his or her option for the current Plan Period will be automatically terminated, and no further Contributions for the purchase of Shares will be made (or will be permitted to be made) during the Plan Period.

(b) Upon termination of the Participating Employee's Continuous Status as an Employee prior to a Plan Period Termination Date for any reason, including retirement or death, the Contributions credited to his or her account will be returned to him or her or, in the case of his or her death, to the person or persons entitled thereto under Section 8, and his or her option will be automatically terminated.

(c) In the event a Participating Employee fails to remain an eligible Employee during the Plan Period in which he or she is a Participating Employee, he or she will be deemed to have elected to withdraw from the Plan and the Contributions credited to his or her account and remaining there will be returned to him or her and his or her option terminated.

(d) A Participating Employee's withdrawal during a Plan Period will not have any effect upon his or her eligibility to participate in a succeeding Plan Period or in any similar plan which may hereafter be adopted by the Company.

7. **No Special Service Rights**

Nothing contained in this Plan shall confer upon any Employee any right with respect to the continuation of his or her employment with the Company or any Covered Entity or any other entity, corporation, partnership, limited liability company or business trust controlling, controlled by or under common control with the Company, or interfere in any way with the right of any such entity, subject to the terms of any separate employment agreement or provision of law or the Company's charter or by-laws to the contrary, at any time to terminate such employment

relationship or to increase or decrease, or otherwise adjust, the other terms and conditions of the Employee's employment.

8. Designation of Beneficiary

8.1. A Participating Employee may file a written designation of a beneficiary who is to receive any Shares and cash, if any, from the Participating Employee's account under the Plan in the event of such Participating Employee's death subsequent to the end of a Plan Period but prior to delivery to him or her of such Shares and cash. Any such beneficiary shall also be entitled to receive any cash from the Participating Employee's account under the Plan in the event of such Participating Employee's death during a Plan Period.

8.2. Such designation of beneficiary may be changed by the Participating Employee at any time by written notice. In the event of the death of a Participating Employee and in the absence of a beneficiary validly designated under the Plan who is living at the time of such Participating Employee's death, the Company shall deliver such Shares and/or cash to the executor or administrator of the estate of the Participating Employee, or if no such executor or administrator has been appointed (to the knowledge of the Company), the Company, in its discretion, may deliver such Shares and/or cash to the spouse or to any one or more dependents or relatives of the Participating Employee, or if no spouse, dependent or relative is known to the Company, then to such other person as the Company may designate.

9. Transferability of Options and Shares

Neither Contributions credited to a Participating Employee's account nor any rights with regard to the exercise of an option or to receive Shares under the Plan may be assigned, transferred, pledged or otherwise disposed of in any way (other than by will, the laws of descent and distribution, or as provided in Section 8) by the Participating Employee. Any such attempt at assignment, transfer, pledge or other disposition shall be without effect, except that the Company may treat such act as an election to withdraw funds in accordance with Section 6.7. In addition, if the Committee has so announced to Participating Employees at least five days prior to the scheduled beginning of the next Plan Period, any Shares acquired on the Plan Period Termination Date of such Plan Period may be subject to restrictions specified by the Committee on the transfer of such Shares. Any Participating Employee selling or transferring any or all of his or her Shares purchased pursuant to the Plan must provide written notice of such sale or transfer to the Company within five business days after the date of sale or transfer. Such notice to the Company shall include the gross sales price, if any, the Plan Period during which the Shares being sold were purchased by the Participating Employee, the number of Shares being sold or transferred and the date of sale or transfer. The Committee may also require that Shares acquired under the Plan be deposited directly into an account established in the name of the Participating Employee with a Company-designated broker and be retained with such designated broker for a specified period of time.

10. Use of Funds

All Contributions received or held by the Company under the Plan may be used by the Company for any corporate purpose, and the Company shall not be obligated to segregate such Contributions from its other assets.

11. Reports

Individual accounts will be maintained for each Participating Employee in the Plan. Statements of account will be given to Participating Employees at least annually, which statements will set forth, with respect to the immediately prior calendar year, the amounts of Contributions, the per Share Purchase Price, the number of Shares purchased and the remaining cash balance, if any.

12. Adjustments Upon Changes in Capitalization; Corporate Transactions

12.1. Adjustment in General. All of the share numbers set forth in the Plan reflect the capital structure of the Company as of the Effective Date. If subsequent to that date the outstanding Shares (or any other securities covered by the Plan by reason of the prior application of this Section) are increased, decreased, or exchanged for a different number or kind of shares or other securities, or if additional shares or new or different shares or other securities are distributed with respect to Shares, as a result of a reorganization, recapitalization, reclassification, stock dividend, stock split, reverse stock split, or other similar distribution with respect to such Shares, an appropriate and proportionate adjustment will be made in (i) the maximum numbers and kinds of shares provided in Section 3, (ii) the numbers and kinds of shares or other securities subject to the then outstanding options, and (iii) the exercise price for each share or other unit of any other securities subject to then outstanding options.

12.2. Adjustment Upon the Occurrence of Certain Unusual or Nonrecurring Events. In the event of any corporate action not specifically covered by the preceding Section 12.1, including but not limited to an extraordinary cash distribution on Common Stock, a corporate separation or other reorganization or liquidation, the Committee may make such adjustment of outstanding options and their terms, if any, as it, in its sole discretion, may deem equitable and appropriate in the circumstances. The Committee may make adjustments in the terms and conditions of, and the criteria included in, options in recognition of unusual or nonrecurring events (including, without limitation, the events described in this Section 12.2) affecting the Company or the financial statements of the Company or of changes in applicable laws, regulations, or accounting principles, whenever the Committee determines that such adjustments are appropriate in order to prevent dilution or enlargement of the benefits or potential benefits intended to be made available under the Plan.

12.3. Related Matters. Any adjustment in options made pursuant to Section 12.1 or 12.2 shall be determined and made, if at all, by the Committee, acting in its sole discretion, and shall include any correlative modification of terms which the Committee may deem necessary or appropriate so as to ensure the rights of the Participating Employees in their respective options are not substantially diminished nor enlarged as a result of the adjustment and corporate action other than as expressly contemplated in this Section 12.

12.4. Corporate Transactions. In the event of a Corporate Transaction that is a dissolution or liquidation of the Company, the Plan Period then in progress will terminate immediately prior to the consummation of such action, unless otherwise provided by the Committee. In the event of any other Corporate Transaction, each option outstanding under the Plan may be assumed or an equivalent option may be substituted by the successor corporation or a parent or subsidiary of such successor corporation. In the event that the successor corporation refuses to assume or substitute for outstanding options, the Plan Period then in progress shall be shortened and a new Plan Period Termination Date shall be set (the "New Plan Period Termination Date"), as of which date the Plan Period then in progress will terminate. The New Plan Period Termination Date shall be on or before the date of consummation of the Corporate

Transaction and the Committee shall notify each Participating Employee in writing, at least three Business Days prior to the New Plan Period Termination Date, that the Plan Period Termination Date for his or her option has been changed to the New Plan Period Termination Date and that his or her option will be exercised automatically on the New Plan Period Termination Date, unless prior to such date he or she has withdrawn from the Plan Period as provided in Section 6.7. For purposes of this Section 12.4, an option granted under the Plan shall be considered assumed, or a substantially equivalent award shall be considered to have been provided in substitution therefor, if following consummation of the Corporate Transaction, the option is assumed and/or exchanged or replaced with another option issued by the acquiring or succeeding entity (or an affiliate thereof) that confers the right to receive upon exercise of such option, for each share of Common Stock subject to the option immediately prior to the consummation of the Corporate Transaction, the consideration (whether cash, securities or other property) received as a result of the Corporate Transaction by holders of Common Stock for each share of Common Stock held immediately prior to the consummation of the Corporate Transaction (and if holders were offered a choice of consideration, the type of consideration chosen by the holders of a majority of the outstanding shares of Stock); *provided however* that if the consideration received in the transaction is not solely common stock of the successor corporation or its parent (as defined in Section 424(e) of the Code), the Committee may, with the consent of the successor corporation, provide for the consideration to be received upon exercise of the option to be solely common stock of the successor corporation or its parent equal in fair market value to the per Share consideration received by holders of Common Stock in the transaction.

13. Settlement of Awards

13.1. Violation of Law. Notwithstanding any other provision of the Plan to the contrary, if, at any time, in the reasonable opinion of the Company, the issuance of Shares pursuant to the Plan may constitute a violation of law, then the Company may delay such issuance of such Shares until (i) approval shall have been obtained from such governmental agencies, other than the Commission, as may be required under any applicable law, rule, or regulation and (ii) in the case where such issuance would constitute a violation of a law administered by or a regulation of the Commission, one of the following conditions shall have been satisfied:

- (a) the Shares are, at the time of the issue of such Shares, effectively registered under the Securities Act; or
- (b) the Company shall have determined, on such basis as it deems appropriate (including an opinion of counsel in form and substance satisfactory to the Company) that the sale, transfer, assignment, pledge, encumbrance or other disposition of such Shares or such beneficial interest, as the case may be, does not require registration under the Securities Act or any applicable state securities laws.

The Company shall make all reasonable efforts to bring about the occurrence of said events.

13.2. Corporate Restrictions on Rights in Stock. Any Shares to be issued pursuant to the Plan shall be subject to all restrictions upon the transfer thereof which may be now or hereafter imposed by the certificate of incorporation and bylaws of the Company.

13.3. Investment Representations. As a condition to the exercise of an option, the Company may require the person exercising such option to represent and warrant at the time of

any such exercise that the Shares are being purchased only for investment and without any present intention to sell or distribute such Shares if, in the opinion of counsel for the Company, such a representation is required by any of the aforementioned applicable provisions of law. The Company shall be under no obligation to issue any Shares unless the Shares to be issued pursuant to the Plan have been effectively registered under the Securities Act.

13.4. Placement of Legends; Stop Orders; etc. Each Share to be issued pursuant to the Plan may bear a reference to any applicable restriction under the Plan. All Shares or other securities delivered under the Plan shall be subject to such stop transfer orders and other restrictions as the Committee may deem advisable under the rules, regulations, and other requirements of any stock exchange upon which the Common Stock is then listed, and any applicable federal or state securities law, and the Committee may cause a legend or legends to be put on any such certificates to make appropriate reference to such restrictions.

13.5. Company Charter and By-Laws; Other Company Policies. This Plan and all options granted under this Plan (including the exercise of an option) are subject to and must comply with the certificate of incorporation and bylaws of the Company, as they may be amended from time to time, and all other Company policies duly adopted by the Board, the Committee or any other committee of the Board as in effect from time to time regarding the acquisition, ownership or sale of Common Stock by employees, including, without limitation, policies intended to limit the potential for insider trading and to avoid or recover compensation payable or paid on the basis of inaccurate financial results or statements, employee conduct, and other similar events.

14. Adopting Subsidiaries

Any Subsidiary of the Company may request that its Employees be allowed to participate in the Plan in accordance with procedures to be adopted by the Board. The Board may, in its sole discretion, approve or reject any such request. Any such Subsidiary whose request is approved by the Board shall be referred to herein as a "Covered Entity." In addition, the Board may determine, in its sole discretion, that a Subsidiary that is a Covered Entity will cease to be a Covered Entity with respect to Plan Periods not yet commenced.

15. Amendment and Termination

(a) The Committee may at any time terminate the Plan or make such modifications of the Plan as it shall deem advisable. Except as provided in Section 12, no termination of the Plan may affect outstanding options, provided that the Plan or a Plan Period may be terminated by the Committee on a Plan Period Termination Date or by the Committee's setting a new Plan Period Termination Date with respect to a Plan Period then in progress if the Committee determines that termination of the Plan and/or any Plan Period is in the best interests of the Company and its stockholders or if continuation of the Plan and/or a Plan Period would cause the Company to incur adverse accounting charges as a result of the Plan. Except as provided in Section 12 or this Section 15, no amendment to the Plan shall make any change in any outstanding option which adversely affects the rights of any Participating Employee.

(b) In addition to the foregoing, without stockholder consent and without regard to whether any Participating Employee rights may be considered to have been adversely affected, the Committee shall be entitled to change the Plan Periods, establish the exchange ratio applicable to amounts withheld in a currency other than U.S. dollars (if applicable), permit

payroll withholding in excess of the amount designated by a Participating Employee to adjust for delays or mistakes in the Company's processing of properly completed withholding elections, establish reasonable waiting and adjustment periods and/or accounting and crediting procedures to ensure that amounts applied toward the purchase of Common Stock for each Participating Employee properly correspond with amounts withheld from the Participating Employee's Compensation, and establish such other limitations or procedures as the Committee determines in its sole discretion advisable which are consistent with the Plan.

16. Notices and Other Communications

Any notice, demand, request or other communication hereunder to any party shall be deemed to be sufficient if contained in a written instrument delivered in person or duly sent by first class registered, certified or overnight mail, postage prepaid, or by facsimile with a confirmation copy by regular, certified or overnight mail, addressed or by facsimile, as the case may be, (i) if to a Participating Employee, at his or her residence address last filed with the Company and (ii) if to the Company, at its principal place of business, addressed to the attention of its Chief Financial Officer, or to such other address or facsimile number, as the case may be, as the addressee may have designated by notice to the addressor. All such notices, requests, demands and other communications shall be deemed to have been received: (i) in the case of personal delivery, on the date of such delivery; (ii) in the case of mailing, when received by the addressee; and (iii) in the case of facsimile transmission, when confirmed by facsimile machine report. In addition, the Company may, in its sole discretion, deliver any documents related to the Plan by electronic means or request that the Participating Employee communicate with the Company with respect to the Plan by electronic means. By participating in the Plan, each Participating Employee will have consented to receive such documents by electronic delivery and, if requested, to agree to participate in the Plan through an on-line or electronic system established and maintained by the Company or another third party designated by the Company, and such consent shall remain in effect throughout the Participating Employee's term of employment or service with the Company and thereafter until withdrawn in writing by the Participant.

17. Governing Law

The Plan and all options and actions taken thereunder shall be governed, interpreted and enforced in accordance with the laws of the State of Delaware without regard to the conflict of laws principles thereof.

18. Term of Plan

The Plan shall become effective on the IPO Date and shall continue in effect until the tenth (10th) anniversary thereof, unless earlier terminated pursuant to Section 15.

[End of document.]

SAMPLE

RHYTHM PHARMACEUTICALS, INC.

2017 EMPLOYEE STOCK PURCHASE PLAN

ENROLLMENT AGREEMENT

- Original Application
- Change in Payroll Deduction Rate
- Change in Beneficiary(ies)

Enrollment Date:

1. I, , hereby elect to participate in the Rhythm Pharmaceuticals, Inc. 2017 Employee Stock Purchase Plan (the "Purchase Plan"), and subscribe to purchase shares of the Company's Common Stock in accordance with this Enrollment Agreement and the Purchase Plan. Capitalized terms used (and not otherwise defined) in this enrollment agreement have the meanings assigned to them in the Purchase Plan.
2. I hereby authorize payroll deductions from each paycheck in the amount of % of my Compensation (from 1% to 15%) on each payroll date during the Plan Period in accordance with the Purchase Plan. (Please note that no fractional percentages are permitted.)
3. I understand that such payroll deductions will be accumulated for the purchase of shares of Common Stock at the applicable purchase price determined in accordance with the Purchase Plan. I understand that, if I do not withdraw from a Plan Period, any accumulated payroll deductions will be used to automatically purchase shares of Common Stock.
4. I understand that all my payroll deductions received or held by the Company under the Purchase Plan may be used by the Company for any corporate purpose, and the Company shall not be obligated to segregate such payroll deductions. Until shares are issued to me, I will only have the rights of an unsecured creditor with respect to such accumulated payroll deductions.
5. I have received a copy of the Purchase Plan Prospectus and the Purchase Plan document. I understand that my participation in the Purchase Plan is in all respects subject to the terms of the Purchase Plan.
6. Shares purchased for me under the Purchase Plan should be issued in the name(s) of (Employee or Employee and spouse only):

7. I understand that if I dispose of any shares received by me pursuant to the Purchase Plan within two years after the Plan Period Commencement Date (the first day of a Plan Period during which I purchased such shares) or one year after the Plan Period Termination Date, I will be treated for federal income tax purposes as having received ordinary income at the time of such disposition in an amount equal to the excess of the fair market value of the shares at the time such shares were purchased by me over the price which I paid for the shares. I hereby agree to notify the Company in writing within five (5) business days after the date of any disposition of my shares, and I will make adequate provision for federal, state or other tax withholding obligations, if any, which arise upon the disposition of the Common Stock. The Company may, but will not be obligated to, withhold from my compensation the amount necessary to meet any applicable withholding obligation, including any withholding necessary to make available to the Company any tax deductions or benefits attributable to the sale or early disposition of Common Stock by me.

If I dispose of such shares at any time after the expiration of the applicable holding periods, I understand that I will be treated for federal income tax purposes as having received income only at the time of such disposition, and that such income will be taxed as ordinary income only to the extent of an amount equal to the lesser of (a) the excess of the fair market value of the shares at the time of such disposition over the purchase price which I paid for the shares or (b) 15% of the fair market value of the shares on the first day of the Plan Period. The remainder of the gain, if any, recognized on such disposition will be taxed as capital gain.

8. I hereby agree to be bound by the terms of the Purchase Plan. The effectiveness of this Enrollment Agreement is dependent upon my eligibility to participate in the Purchase Plan.

9. I hereby agree to establish a brokerage account with [REDACTED] and to fill out and submit the necessary forms to allow the Company to deposit shares purchased on my behalf under the Purchase Plan in such account, if I have not done so already.]

10. In the event of my death, I hereby designate the following as my beneficiary(ies) to receive all payments and shares due me under the Purchase Plan:

BENEFICIARY NAME: (Please print)

(First)

(Middle)

(Last)

Relationship

2

I UNDERSTAND THAT THIS ENROLLMENT AGREEMENT SHALL REMAIN IN EFFECT THROUGHOUT SUCCESSIVE PLAN PERIODS UNLESS TERMINATED BY ME.

Dated:

Signature of Employee

Print name

Spouse's Signature
(If beneficiary other than spouse)

3

SAMPLE

RHYTHM PHARMACEUTICALS, INC.

2017 EMPLOYEE STOCK PURCHASE PLAN

NOTICE OF WITHDRAWAL

The undersigned participant in the Rhythm Pharmaceuticals, Inc. 2017 Employee Stock Purchase Plan, hereby notifies the Company that he or she hereby withdraws from the Plan Period beginning [REDACTED]. He or she hereby directs the Company to pay to the undersigned as promptly as practicable all the payroll deductions credited to his or her account with respect to such Plan Period. The undersigned understands and agrees that his or her option for such Plan Period will be automatically terminated, that no further payroll deductions will be made for the purchase of shares in the current Plan Period, and that the undersigned shall be eligible to participate in subsequent Plan Periods only by delivering to the Company a new Enrollment Agreement.

Name: _____

Signature: _____

Date: _____



Rhythm Pharmaceuticals, Inc.
500 Boylston Street — 11th Floor
Boston, MA 02116
Main Telephone: 617-585-2090
www.rhythmtx.com

September 13, 2017

Keith M. Gottesdiener, M.D.
c/o Rhythm Pharmaceuticals, Inc.
500 Boylston Street, 11th Floor
Boston, MA 02116

Dear Keith:

On behalf of Rhythm Pharmaceuticals, Inc., formerly known as Rhythm Metabolic, Inc. (the “Company” or “Rhythm”), I am pleased to set forth below the amended and restated terms of your employment with the Company.

Employment. You are currently the Chief Executive Officer and President of the Company, and during the term of your employment with the Company, you will continue to hold the positions and titles of Chief Executive Officer and President. During the term of your employment with the Company, you will be responsible for performing the duties associated with the position above or as the Company may otherwise assign to you. Your primary place of employment initially will be in the Company’s offices located in Boston, Massachusetts; however, you will be expected to travel as may be necessary to fulfill your responsibilities. In the course of your employment with the Company, you will be subject to, and required to comply with, all Company policies and all applicable laws and regulations.

Base Salary. During your employment, your salary will be \$490,795 annualized, subject to all required and elected taxes and other withholdings. Your salary may be adjusted from time to time in accordance with normal business practice and in the sole discretion of the Company.

Annual Incentive Bonus. Following the end of each fiscal year and subject to the approval by the Company’s Board of Directors, you will be eligible to earn an incentive bonus, based on your performance and the Company’s performance, each during the applicable fiscal year, if your employment continues in good standing on the date of payment of such incentive bonus. Your target annual incentive bonus opportunity is 50% of your annualized base salary.

Equity Grant. Any existing grants of equity you have in the Company will be treated consistent with the terms of the applicable agreements under which such awards have been granted. You may be awarded additional equity grants from time to time in accordance with normal business practice and in the sole

discretion of the Company’s Board of Directors. The terms of any future equity grant will be consistent with any plan under which they are granted and the terms of the applicable agreement for the award(s).

Benefits. You may participate in any and all benefit programs that the Company establishes and makes available to its employees from time to time, subject to the terms and conditions of those programs. The Company’s benefits programs are subject to change at any time in the Company’s sole discretion.

Vacation. You will be entitled to annual paid vacation of four (4) weeks. Your accrual and use of vacation time will be pursuant to any vacation or time off policy the Company may establish or modify from time to time. The Company’s vacation policy is subject to change at any time in the Company’s sole discretion.

Severance. If the Company terminates your employment without Cause (as defined below) or you resign your employment with the Company for Good Reason (as defined below) (in either event, a “Qualifying Termination”), then, subject to your execution of a reasonable release acceptable to the Company (the “Release”), the expiration of any revocation period provided in the Release and your continued compliance with the terms of the NDA (as defined below), the Company will pay you an amount equal to your then-current base salary rate for a period of twelve (12) months (the “Regular Severance Amount”).

If there is a Qualifying Termination within the three (3) months immediately preceding or the twelve (12) months immediately following a Change of Control (as defined in the Company’s 2015 Equity Incentive Plan, as may be amended and in effect from time to time or succeeded or superseded by a successor equity incentive plan), then, subject to your execution of a Release following your Separation from Service (as defined below), the expiration of any revocation period provided in the Release and your continued compliance with the terms of the NDA, the Company will pay you, in lieu of any Regular Severance Amount, an amount (the “Change of Control Severance Amount”) equal to your then-current base salary rate for a period of twelve (12) months plus an amount equal to 100% of your then-applicable target annual incentive bonus, provided that, if any such Qualifying Termination contemplated under the foregoing provisions of this paragraph occurs at any time after the closing of the Company’s first underwritten public offering of its Common Stock under the Securities Act, if any, the Change of Control Severance Amount shall be an amount equal to your then-current base salary rate for a period of eighteen (18) months plus an amount equal to 100% of your then-applicable target annual incentive bonus.

Any severance amount to which you may be entitled under this letter will be paid in substantially equal installments in accordance with the Company’s ordinary payroll practices, beginning on the first payroll date following the date that is either (i) sixty (60) days after the date of your Separation from Service

or (ii) in the case of a Separation from Service that is a Qualifying Termination that occurs within three (3) months immediately preceding a Change of Control, sixty (60) days after such Change of Control, provided that, in the case of either of the foregoing clauses (i) and (ii), the Company, in its sole discretion, may have the option to pay any such severance amount to you as a lump sum. To be eligible for either the Regular Severance Amount or the Change of Control Severance Amount, as applicable, you must execute and deliver the Release to the Company and allow it to become effective within thirty (30) days of your Separation from Service or, if later, within thirty (30) days of a Change of Control giving rise to a Change of Control Severance Amount entitlement.

In addition, if following your Separation from Service, you are eligible for and timely elect continued medical insurance coverage pursuant to COBRA, the Company will reimburse you for the applicable premiums for you and your eligible dependents during the period commencing on the date of your Separation from Service and ending on the earlier to occur of (a) the final day of the applicable severance period and (b) the date you otherwise become ineligible for continued coverage under COBRA. Notwithstanding the foregoing, if the Company determines that it cannot provide such reimbursement of premiums to you without potentially violating applicable law, the Company shall not be obligated to make any such payments or reimbursements to you.

If the Qualifying Termination occurs within the three (3) months immediately preceding or the twelve (12) months immediately following a Change of Control, then each outstanding equity award in the Company held by you shall immediately vest and, if applicable, become exercisable with respect to one hundred percent (100%) of the shares of equity of the Company subject thereto. The foregoing provisions of this paragraph shall apply notwithstanding anything express or implied to the contrary in any agreement or award between you and the Company, or in any plan of the Company, that is applicable to such outstanding equity award.

Notwithstanding anything herein to the contrary, in the event that any compensation or benefit that constitutes “nonqualified deferred compensation” within the meaning of Section 409A of the Internal Revenue Code of 1986, as amended (the “Code”), becomes payable upon the occurrence of a Change of Control, such compensation or benefit shall not be paid unless such Change of Control constitutes a “change in control event” within the meaning of Section 409A of the Code.

If any payment or benefit you would receive under this letter, when combined with any other payment or benefit you receive pursuant to the termination of your employment with the Company (“Payment”) would (i) constitute a “parachute payment” within the meaning of Section 280G of the Code, and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the “Excise Tax”), then such Payment shall be either (x) the full amount of such Payment or (y) such lesser amount (with your choice of whether to reduce cash payments or stock option compensation or both) as would result in no portion of the Payment being subject to the Excise Tax, whichever of the foregoing amounts, taking into account the applicable federal, state and local employment taxes, income taxes and the Excise Tax results in your receipt, on an after-tax basis, of the greater amount of the Payment notwithstanding that all or some portion of the Payment may be subject to the Excise Tax.

Definitions

Separation from Service. For purposes of this letter, “Separation from Service” means a “separation from service” within the meaning of Section 409A of the Code. Each installment payment provided under this letter shall at all times be considered a separate and distinct payment for purposes of Section 409A of the Code. Notwithstanding anything in this letter to the contrary, to the extent required to avoid a prohibited distribution under Section 409A of the Code, the benefits provided under this letter will not be provided to you until the earlier of (a) the expiration of the six-month period measured from the date of your Separation from Service with the Company or (b) the date of your death. Upon the first business day after expiration of the relevant period, all payments delayed pursuant to the preceding sentence will be paid in a lump sum and any remaining payments due will be paid as otherwise provided herein.

Cause. “Cause” shall mean the occurrence of any of the following events by the individual: (i) commission of any crime involving the Company, or any crime involving fraud, breach of trust, or physical or emotional harm to any person, moral turpitude or dishonesty; (ii) any unauthorized use or disclosure of the Company’s proprietary information (other than any such use or disclosure that is not intentional and is not material); (iii) any intentional misconduct or gross negligence that has a material adverse effect on the Company’s business or reputation; (iv) any material breach by you of any agreement between you and the Company that is not cured within thirty (30) days after receipt of written notice from the Company describing any such breach; or (v) repeated and willful failure to perform the duties, functions and responsibilities of the individual’s position after a written warning from the Company.

Good Reason. “Good Reason” shall mean your resignation from all positions you then hold with the Company if: (A) without your written consent (i) there is a material diminution in the nature or scope of your responsibilities, duties, authority, or title; (ii) there is a material reduction of your base salary; provided, however, that a material reduction in your base salary pursuant to a salary reduction program affecting all or substantially all of the employees of the Company and that does not adversely affect you to a greater extent than other similarly situated employees shall not constitute Good Reason; or (iii) you are required to relocate your primary work location to a facility or location that would increase your one way commute distance by more than thirty-five (35) miles from your primary work location as of immediately prior to such change, (B) you provide written notice outlining such conditions, acts or omissions to the Company’s Chairman of the Board, Chief Financial Officer, or General Counsel within thirty (30) days immediately following such material change or reduction, (C) such material change or reduction is not remedied by the Company within thirty (30) days following the Company’s receipt of such written notice and (D) your resignation is effective not later than thirty (30) days after the expiration of such thirty (30) day cure period. “Good Reason” shall also mean your resignation on the one year anniversary of a Change of Control from all positions you then hold with the Company or its successor if by that date you have not entered into a written letter or agreement with the Company or such successor that provides for your continued employment with the Company or such successor. For purposes of clarification, any Qualifying Termination that occurs on the first anniversary of a Change of Control shall be deemed and treated as occurring within the twelve (12) months immediately following a Change of Control for all purposes of this letter.

Invention, Non-Disclosure, Non-Competition and Non-Solicitation Obligations. You previously have executed and delivered the Company’s standard form of Employee Proprietary Information, Inventions, Non-Competition and Non-Solicitation Agreement (the “NDA”), an executed copy of which is attached hereto as Exhibit A.

At-Will Employment. This letter shall not be construed as an agreement, either express or implied, to employ you for any stated term, and shall in no way alter the Company’s policy of employment at-will. Similarly, nothing in this letter shall be construed as an agreement, either express or implied, to pay you

any compensation or grant you any benefit beyond the end of your employment with the Company, except as otherwise explicitly set forth in this letter. This letter supersedes all prior understandings, whether written or oral, including, without limitation, your current employment agreement, with respect to the subject matter of this letter.

[The remainder of this page is intentionally left blank.]

Please indicate your acceptance of this letter agreement by signing below in the space provided for your signature.

Sincerely,

/s/ David Meeker

David Meeker
Chairman of the Board

The foregoing correctly sets forth the terms of my at-will employment with the Company. I am not relying on any representations other than those set forth above.

/s/ Keith M. Gottesdiener

September 13, 2017

Keith M. Gottesdiener, M.D.

Date



EXHIBIT A

EXECUTED NDA

[See attached]

RHYTHM PHARMACEUTICALS, INC.

**EMPLOYEE PROPRIETARY INFORMATION, INVENTIONS, NON-COMPETITION
AND NON-SOLICITATION AGREEMENT**

In consideration and as a condition of my employment, or continued employment, by Rhythm Pharmaceuticals, Inc., a Delaware corporation (the “Company”), and the compensation now and hereafter paid to me, I hereby agree as follows:

1. nondisclosure

1.1 Recognition of Company’s Rights; Nondisclosure. At all times during my employment by the Company and thereafter, I will hold in strictest confidence and will not disclose, use, lecture upon, or publish any of the Company’s Proprietary Information (defined below), except as such disclosure, use, lecture, or publication may be required in connection with my work for the Company, or unless any other individual that is an officer of the Company expressly authorizes such in writing. I will obtain the Company’s prior written approval before publishing or submitting for publication any material (written, oral, or otherwise) that relates to my work at the Company or incorporates any Proprietary Information. Notwithstanding the foregoing, disclosure of any such Proprietary Information shall not be prohibited if such disclosure is directly related to a valid and existing order of a court or other governmental body or agency; provided, however, that I shall have first given prompt notice to the Company of any possible or prospective order and the Company shall have been afforded a reasonable opportunity to prevent or limit any such disclosure. I hereby assign to the Company any rights I may have or acquire in any Proprietary Information and recognize that all Proprietary Information shall be the sole property of the Company and its assigns.

1.2 Proprietary Information. The term “Proprietary Information” means any and all confidential or proprietary knowledge, data or information of the Company or any of its subsidiaries or controlled affiliates. By way of illustration but not limitation, “Proprietary Information” includes: (a) developments, inventions, ideas, data, programs, other works of authorship, designs and techniques, trade secrets, mask works, processes, formulas, source and object codes, algorithms, compositions of matter, chemical structures, formulations, methods (including, without limitation, methods of use, delivery or manufacture), dosing regimens, know-how, technology, improvements and discoveries (hereinafter collectively referred to as “Inventions”); (b) the design of, and all other information with respect to, preclinical studies and clinical trials, including, without limitation, the results of such preclinical studies and clinical trials; (c) clinical development and regulatory approval strategy; (d) information regarding research collaborations, joint development relationships, licensing relationships and transactions, corporate partnering relationships and transactions, joint ventures and other strategic alliances, including, without limitation, the research, development and commercialization activities, areas or fields subject to such relationships or transactions, the results of such research, development or commercialization activities and the terms of any agreements entered into by the Company or any of its subsidiaries or controlled affiliates in connection with such relationships or transactions; (e) information regarding plans for research, development, new services or products, marketing and

subsidiaries or controlled affiliates. For purposes of this Employee Proprietary Information, Inventions, Non-Competition and Non-Solicitation Agreement (this “Agreement”), the term “Proprietary Information” shall not include information which is or becomes publicly available without breach of: (i) this Agreement; (ii) any other agreement or instrument to which the Company or any of its subsidiaries or controlled affiliates is a party or a beneficiary; or (iii) any duty owed to the Company or any of its subsidiaries or controlled affiliates by me or by any third party; *provided, however*, that if I shall seek to disclose, use, lecture upon, or publish any Proprietary Information, I shall bear the burden of proving that any such information shall have become publicly available without any such breach.

1.3 Third Party Information. I understand that the Company or any of its subsidiaries or controlled affiliates has received and in the future will receive from third parties confidential or proprietary information (“Third Party Information”) subject to a duty to maintain the confidentiality of such information and to use it only for certain limited purposes. During the term of my employment by the Company and thereafter, I will hold Third Party Information in the strictest confidence and will not disclose Third Party Information to anyone (other than personnel of the Company or any of its subsidiaries or controlled affiliates who need to know such information in connection with their work for the Company or any of its subsidiaries or controlled affiliates) and will not use Third Party Information (except in connection with my work for the Company or any of its subsidiaries or controlled affiliates), unless and to the extent that any other individual that is an officer of the Company expressly authorizes such disclosure or use in writing. I hereby assign to the Company any rights I may have or acquire in any Third Party Proprietary Information during my employment with the Company.

1.4 No Improper Use of Information of Prior Employers and Others. During my employment by the Company, I will not improperly use or disclose any confidential information or trade secrets, if any, of any former employer or any other person to whom I have an obligation of confidentiality, and I will not bring onto the premises of the Company or any of its subsidiaries or controlled affiliates any unpublished documents or any property belonging to any former employer or any other person to whom I have an obligation of confidentiality unless consented to in writing by that former employer or person. I will use in the performance of my duties only information which is generally known and used by persons with training and experience comparable to my own, which is common knowledge in the industry or otherwise legally in the public domain, or which is otherwise provided or developed by, or on behalf of, the Company or any of its subsidiaries or controlled affiliates.

1.5 Defend Trade Secrets Act. Pursuant to 18 U.S.C. § 1833(b), I will not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of a trade secret of the Company or its affiliates that (a) I make (i) in confidence to a Federal, State, or local government official, either directly or indirectly, or to my attorney and (ii) solely for the purpose of reporting or investigating a suspected violation of law; or (b) I make in a complaint or other document that is filed under seal in a lawsuit or other proceeding. If I file a lawsuit for retaliation by the Company for reporting a suspected violation of law, I may disclose the trade secret to my attorney and use the trade secret information in the court proceeding, if I (x) file any document containing the trade secret under seal, and (y) do not disclose the trade secret, except pursuant to court order. Nothing in this Agreement is intended to conflict with 18 U.S.C. § 1833(b) or create liability for disclosures of trade secrets that are expressly allowed by 18 U.S.C. § 1833(b).

2. ASSIGNMENT OF INVENTIONS

2.1 Proprietary Rights. The term “Proprietary Rights” means all trade secret, patent, copyright, mask work and other intellectual property rights throughout the world.

2.2 Prior Inventions. Inventions, if any, patented or unpatented, which I made prior to the commencement of my employment with the Company are excluded from the scope of this Agreement. To preclude any possible uncertainty, I have set forth on Exhibit A (Prior Inventions) attached hereto a complete list of all Inventions that I have, alone or jointly with others, conceived, developed or reduced to practice or caused to be conceived, developed or reduced to practice prior to the commencement of my employment with the Company, that I consider to be my property or the property of third parties and that I wish to have excluded from the scope of this Agreement (collectively referred to as “Prior Inventions”). If disclosure of any such Prior Invention would cause me to violate any prior confidentiality agreement, I understand that I am not to list such Prior Inventions in Exhibit A but am only to disclose a cursory name for each such invention, a listing of the party or parties to whom it belongs, and the fact that full disclosure as to such inventions has not been made for that reason. A space is provided on Exhibit A for such purpose. If I do not attach such disclosure, I am representing thereby that there are no Prior Inventions. If, in the course of my employment with the Company, I incorporate a Prior Invention (whether or not such Prior Invention is listed in Exhibit A) into a product, compound, composition of matter, chemical structure, biological material, formulation, method, process or machine of the Company or any of its subsidiaries or controlled affiliates, or I in any way otherwise use, or make available for use, a Prior Invention (whether or not such Prior Invention is listed in Exhibit A) in connection with the research, development, manufacture, use or commercialization of any such product, compound, composition of matter, chemical structure, biological material, formulation, method, process or machine, the Company is hereby granted and shall have a nonexclusive, royalty free, irrevocable, perpetual, worldwide license (with rights to sublicense through multiple tiers of sublicensees) to research, cause to be researched, develop, cause to be developed, make, cause to be made, modify, cause to be modified, use, cause to be used and sell or otherwise commercialize, or cause to be sold or otherwise commercialized, such Prior Invention. Notwithstanding the foregoing, I agree that I will not incorporate, or permit to be incorporated, Prior Inventions in any Company Inventions (as defined in Section 2.3 below), or in any product, compound, composition of matter, chemical structure, biological material, formulation, method, process or machine of the Company or any of its subsidiaries or controlled affiliates, without the Company’s prior written consent.

2.3 Assignment of Inventions. Subject to this Section 2.3 and to Sections 2.5 and 2.6, I hereby assign to the Company all my right, title and interest in and to any and all Inventions (and all Proprietary Rights with respect thereto), whether or not patentable or registrable under copyright or similar statutes, that are made, conceived, reduced to practice or learned by me, either alone or jointly with others, (i) in the course of my employment with the Company, (ii) during the term of my employment with the Company (whether or not in the course of my employment with the Company and whether or not during regular business hours) if and to the extent that any such Invention relates to the actual business or planned business of the Company or was made, conceived or reduced to practice by me, either alone or jointly with others, as a result of any material use of any of the properties, assets or facilities of the Company or (iii) arising out of, based upon, or resulting from the use of, any Proprietary Information or Third-Party Proprietary Information made available to me or to which I had access as an

employee of the Company. Inventions assigned pursuant to this Section 2 to the Company, or to a third party as directed by the Company pursuant to Section 2.5 below, are hereinafter referred to as "Company Inventions." At the request of the Company at any time and from time to time, I will execute and deliver any and all instruments, documents and agreements reasonably requested by the Company for purposes of confirming my assignment to the Company of all of my right, title and interest in and to any and all Company Inventions (and all Proprietary Rights with respect thereto), including, without limitation, at any time when any such Company Inventions (or any Proprietary Rights with respect thereto) are first reduced to practice or first fixed in a tangible medium, as applicable.

For the avoidance of doubt, notwithstanding any contrary provision contained herein, nothing contained in this Agreement shall require the assignment of any Invention (or Proprietary Right with respect thereto) made or conceived by me during the period of my employment to the extent such assignment is prohibited by any applicable state or federal law.

2.4 Obligation to Keep Company Informed. During the period of my employment with the Company and thereafter, I will promptly disclose to the Company fully and in writing all Company Inventions authored, conceived or reduced to practice by me, either alone or jointly with others. In addition, during the period of my employment with the Company and thereafter, I will promptly disclose to the Company all patent applications filed by me or on my behalf that claim any Company Invention.

2.5 Government or Third Party. I also agree to assign all my right, title and interest in and to any particular Company Invention to a third party, including without limitation the United States, as directed by the Company.

2.6 Works for Hire. I acknowledge that all original works of authorship which are made by me (solely or jointly with others) within the scope of my employment with the Company and which are protectable by copyright are "works made for hire," pursuant to the United States Copyright Act (17 U.S.C., Section 101).

2.7 Enforcement of Proprietary Rights. I will assist the Company in every proper way in obtaining, and from time to time enforcing, United States and foreign Proprietary Rights relating to Company Inventions in any and all countries. To that end I will promptly execute, verify and deliver such documents and perform such other acts (including appearances as a witness) as the Company may reasonably request for use in applying for, obtaining, perfecting, evidencing, sustaining and enforcing such Proprietary Rights and the assignment thereof. In addition, I will promptly execute, verify and deliver assignments of such Proprietary Rights to the Company or its designee. My obligation to assist the Company with respect to Proprietary Rights relating to such Company Inventions in any and all countries shall continue beyond the termination of my employment with the Company, but the Company shall compensate me at a reasonable rate after my termination for the time actually spent by me at the Company's request on such assistance.

In the event the Company is unable for any reason, after reasonable effort, to secure my signature on any document needed in connection with the actions specified in the preceding paragraph, I hereby irrevocably designate and appoint the Company and its duly authorized officers and agents as my agents and attorneys-in-fact, subject to full power or substitution and resubstitution, which appointment is coupled with an interest, to act for and in my behalf to execute, verify and

file any such documents and to do all other lawfully permitted acts to further the purposes of the preceding paragraph with the same legal force and effect as if executed by me. I hereby waive and quitclaim to the Company any and all claims, of any nature whatsoever, which I now or may hereafter have for infringement of any Proprietary Rights assigned hereunder to the Company.

3. RECORDS. I agree to keep and maintain adequate and current records (in the form of notes, memoranda, sketches, drawings and in any other form that may be required by the Company) of all Proprietary Information and all Company Inventions made, conceived, developed or reduced to practice by me, which records shall be available to and remain the sole property of the Company at all times.

4. NON-SOLICITATION. I agree that, during the period of my employment with the Company and for the one (1) year period after the date my employment with the Company ends for any reason, including but not limited to voluntary termination by me or termination by the Company, I will not, for myself or for the benefit of any other person (including, without limitation, any other person with which I may have a direct or indirect interest or relationship as an employee, consultant, advisor, equityholder or otherwise): (a) solicit, hire or engage, or attempt to solicit, hire or engage, any individual as an employee, consultant, advisor, officer, manager, managing partner, director or in any other similar capacity if such individual shall have been an employee of the Company or any of its subsidiaries or controlled affiliates at any time during the one (1) year period prior to the date of termination of my employment with the Company; (b) solicit, induce or attempt to induce any customer, vendor, contractor, consultant or advisor of the Company or any of its subsidiaries or controlled affiliates to terminate, diminish, or materially alter his, her or its relationship with the Company or any of its subsidiaries or controlled affiliates; or (c) solicit, induce or attempt to induce any potential customer, vendor, contractor, employee, consultant or advisor whose identity and potential relationship with the Company or any of its subsidiaries or controlled affiliates I learned as a result of my employment with the Company, not to establish, or to diminish or materially alter, such potential relationship with the Company or any of its subsidiaries or controlled affiliates. In the event that a court finds this Section 4, or any of its restrictions, to be unenforceable or invalid, I and the Company agree that (i) this Section 4 will be automatically modified to provide the Company with the maximum protection of its business interests allowed by law and (ii) I shall be bound, and such court shall enforce, this Section 4 as so modified.

5. NON-COMPETITION. I agree that, during the term of my employment with the Company and for the one (1) year period after the date my employment with the Company ends for any reason, including but not limited to voluntary termination by me or termination by the Company, I will not, directly or indirectly, as an officer, director, manager, employee, consultant, advisor, owner, partner, member, stockholder, or in any other capacity, (a) compete with the business or planned business of the Company or any of its subsidiaries or controlled affiliates, or (b) take any steps or actions to facilitate or prepare for competition with the business or planned business of the Company or any of its subsidiaries or controlled affiliates, nor will I assist another person to take any action that I would be prohibited from taking under this Section 5. The obligations not to compete that I have undertaken under this Section 5 shall apply in all countries of the world. For purposes of this Section 5, I will not be deemed or treated as being in competition with the business or planned business of the Company or any of its subsidiaries or controlled affiliates or as being in violation of the covenant set forth in the clause (b) above in this Section 5 merely by virtue of my ownership of any equity interest in any business or person that is in

competition with, or is planning to be in competition with, the business or planned business of the Company or any of its subsidiaries or controlled affiliates, if my ownership of any such equity interest represents five percent (5%) or less the total equity interests in such business or person. I hereby acknowledge and agree that the foregoing restrictions contained in this Section 5 are reasonable, proper and necessitated by the legitimate business interests of the Company and will not prevent me from earning a living or pursuing my career. In the event that a court finds this Section 5, or any of its restrictions, to be unenforceable or invalid, I and the Company agree that (i) this Section 5 will be automatically modified to provide the Company with the maximum protection of its business interests allowed by law and (ii) I shall be bound, and such court shall enforce, this Section 5 as so modified.

The parties agree that for the purposes of this Agreement, "Business" shall mean development of small peptide MC4R agonists for the treatment of human disease.

6. NO CONFLICTING OBLIGATION. I represent that my performance of all the terms of this Agreement and as an employee of the Company has not breached, and does not and will not breach, any agreement to keep in confidence information acquired by me in confidence or in trust prior to, or outside the scope of, my employment by the Company and any agreement not to compete with the business of any third party. I have not entered into, and I agree I will not enter into, any agreement, either written or oral, in conflict herewith.

7. RETURN OF COMPANY DOCUMENTS. When I leave the employ of the Company, I will deliver to the Company any and all notes, memoranda, specifications, drawings, devices, formulas, and documents, together with all copies thereof, and any other material containing or disclosing any Company Inventions, Third Party Information or Proprietary Information of the Company. I further agree that, during the term of my employment with the Company or at any time thereafter, any property situated on the premises of the Company or any of its subsidiaries or controlled affiliates, including disks and other storage media, filing cabinets or other work areas, is subject to inspection by Company personnel at any time with or without notice. In the event I leave the employ of the Company for any reason whatsoever, I will promptly sign and deliver the "Termination Certificate" attached hereto as *Exhibit B*.

8. LEGAL AND EQUITABLE REMEDIES. Because my services are personal and unique and because I may have access to and become acquainted with the Proprietary Information of the Company, the Company shall have the right to enforce this Agreement and any of its provisions by injunction, specific performance, or other equitable relief, without bond and without prejudice to any other rights and remedies that the Company may have for a breach of this Agreement. In the event that the Company enforces the provisions of Section 4 or Section 5 hereof through a court order, I agree that the restrictions contained in Section 4 or Section 5, as the case may be, shall remain in effect for a period of one year from the effective date of such court order. I agree that if the Company is successful in whole or in part in any legal or equitable action against me under this Agreement, the Company shall be entitled to recover from me all costs, including reasonable attorney's fees, incurred by the Company in connection with such legal or equitable action.

9. NOTICES. Any notices required or permitted hereunder shall be given to the appropriate party at the address specified below or at such other address as the party shall specify in writing. Such notice shall be deemed given upon personal delivery to the appropriate address, one (1)

business day after dispatch if sent by nationally recognized courier or overnight delivery service, on the date of dispatch if sent by facsimile or electronic mail for which confirmation of transmission is provided or, if sent by certified or registered mail, three (3) business days after the date of mailing.

10. NOTIFICATION OF NEW EMPLOYER. In the event that I leave the employ of the Company and accept new employment, I hereby agree to notify my new employer of my rights and obligations under this Agreement and I hereby consent to the Company or any person on behalf of the Company providing notice to my new employer of such rights and obligations.

11. GENERAL PROVISIONS

11.1 Governing Law; Consent to Personal Jurisdiction. This Agreement will be governed by and construed according to the laws of the Commonwealth of Massachusetts, as such laws are applied to agreements entered into and to be performed entirely within Massachusetts between Massachusetts residents. I hereby expressly consent to the personal jurisdiction of the state and federal courts located in the Commonwealth of Massachusetts for any lawsuit filed there against me by the Company arising from or related to this Agreement.

11.2 Severability. In case any one or more of the provisions contained in this Agreement shall, for any reason, be held to be invalid, illegal, or unenforceable in any respect, such invalidity, illegality, or unenforceability shall not affect the other provisions of this Agreement, and this Agreement shall be construed as if such invalid, illegal, or unenforceable provision had never been contained herein. Moreover, if any one or more of the provisions contained in this Agreement shall for any reason be held to be excessively broad as to duration, geographical scope, activity or subject, it shall be construed by limiting and reducing it, so as to be enforceable to the extent compatible with the applicable law as it shall then appear.

11.3 Successors and Assigns. This Agreement will be binding upon my heirs, executors, administrators and other legal representatives and will be for the benefit of the Company, its successors, and its assigns. Without limiting the generality of the foregoing, if I become an employee of any subsidiary or controlled affiliate of the Company, then (i) such subsidiary or controlled affiliate shall be deemed and treated as an intended third party beneficiary of this Agreement to the same extent as if such subsidiary or controlled affiliate were a party to this Agreement and (ii) each reference in this Agreement to the term "Company" shall be deemed to be a reference to whichever of Rhythm Pharmaceuticals, Inc. and/or such subsidiary, parent or controlled affiliate is my employer.

11.4 Survival. The provisions of this Agreement shall survive the termination of my employment with the Company and the assignment of this Agreement by the Company to any successor in interest or other assignee.

11.5 Employment. I agree and understand that nothing in this Agreement shall confer any right with respect to continuation of my employment by the Company, nor shall it interfere in any way with my right or the Company's right to terminate my employment at any time, with or without cause.

11.6 Waiver. No waiver by the Company of any breach of this Agreement shall be a waiver of any preceding or succeeding breach. No waiver by the Company of any right under

this Agreement shall be construed as a waiver of any other right. The Company shall not be required to give notice to enforce strict adherence to all terms of this Agreement.

11.7 Entire Agreement. My obligations, and the Company's rights, under this Agreement shall apply to any time during which I was previously employed, or am in the future employed, by the Company. This Agreement is the final, complete and exclusive agreement of the parties with respect to the subject matter hereof and supersedes all prior agreements relating to the subject matter hereof and merges all prior discussions between us. No modification of or amendment to this Agreement, nor any waiver of any rights under this Agreement, will be effective unless in writing and signed by the party to be charged. Any subsequent change or changes in my duties, salary or compensation will not affect the validity or scope of this Agreement.

11.8 Counterparts. This Agreement may be signed in counterparts, each shall be deemed an original and shall together constitute one agreement.

11.9 Acknowledgement. I acknowledge that this Agreement is a condition to my employment with the Company and that I have had a full and adequate opportunity to read, understand and discuss with my advisors, including legal counsel, the terms and conditions contained in this Agreement prior to signing hereunder.

This Agreement shall be effective as of the first day of my employment with the Company.

[Remainder of page intentionally left blank]

I HAVE READ THIS AGREEMENT CAREFULLY AND UNDERSTAND ITS TERMS. I HAVE COMPLETELY FILLED OUT EXHIBIT A TO THIS AGREEMENT.

Dated: 11/16/16

/s/ Keith Gottesdiener

Name: Keith Gottesdiener
Address: 900 5th Ave, Apt 8C
New York, NY 10021

ACCEPTED AND AGREED:

RHYTHM PHARMACEUTICALS, INC.

By: /s/ Bart Henderson

Name: Bart Henderson
Title: President

Dated:

EXHIBIT A

TO: Rhythm Pharmaceuticals, Inc.

FROM:

DATE:

SUBJECT: Prior Inventions

1. Except as listed in Section 2 below, the following is a complete list of all inventions or improvements relevant to the subject matter of my employment by Rhythm Pharmaceuticals, Inc. (the "Company") that have been made or conceived or first reduced to practice by me alone or jointly with others prior to my employment by the Company:
 - o No inventions or improvements.

- See below:
 - Additional sheets attached.
2. Due to a prior confidentiality agreement, I cannot complete the disclosure under Section 1 above with respect to inventions or improvements generally listed below, the proprietary rights and duty of confidentiality with respect to which I owe to the following party(ies):
- | Invention or Improvement | Party(ies) | Relationship |
|--------------------------|------------|--------------|
| 1. | | |
| 2. | | |
| 3. | | |
- Additional sheets attached.
3. I acknowledge that this Exhibit A, if completed, forms a part of the Employee Proprietary Information, Inventions, Non-Competition and Non-Solicitation Agreement to which the Company and I are parties and that the failure to complete this Exhibit A and cause it to be attached to such Agreement constitutes a representation by me that I have no Prior Inventions.
-

EXHIBIT B

TERMINATION CERTIFICATE

I hereby confirm and certify to the Company that I have returned to the Company all Proprietary Information in my possession or control, that I have disclosed fully to the Company all Company Inventions and that I have and will comply fully with all of my obligations to the Company under my Employee Proprietary Information, Inventions, Non-Competition and Non-Solicitation Agreement with the Company.

Name:



Rhythm Pharmaceuticals, Inc.
500 Boylston Street — 11th Floor
Boston, MA 02116
Main Telephone: 617-585-2090
www.rhythmtx.com

September 13, 2017

Fred Fiedorek
c/o Rhythm Pharmaceuticals, Inc.
500 Boylston Street, 11th Floor
Boston, MA 02116

Dear Fred:

On behalf of Rhythm Pharmaceuticals, Inc., formerly known as Rhythm Metabolic, Inc. (the “Company” or “Rhythm”), I am pleased to set forth below the amended and restated terms of your employment with the Company.

Employment. You are currently the Chief Medical Officer of the Company, and during the term of your employment with the Company, you will continue to hold the position and title of Chief Medical Officer. During the term of your employment with the Company, you will be responsible for performing the duties associated with the position above or as the Company may otherwise assign to you. Your primary place of employment initially will be in the Company’s offices located in Boston, Massachusetts; however, you will be expected to travel as may be necessary to fulfill your responsibilities. In the course of your employment with the Company, you will be subject to, and required to comply with, all Company policies and all applicable laws and regulations.

Base Salary. During your employment, your salary will be \$354,732 annualized, subject to all required and elected taxes and other withholdings. Your salary may be adjusted from time to time in accordance with normal business practice and in the sole discretion of the Company.

Annual Incentive Bonus. Following the end of each fiscal year and subject to the approval by the Company’s Board of Directors, you will be eligible to earn an incentive bonus, based on your performance and the Company’s performance, each during the applicable fiscal year, if your employment continues in good standing on the date of payment of such incentive bonus. Your target annual incentive bonus opportunity shall be 30% of your annualized base salary, provided that, from and after the closing of the Company’s first underwritten public offering of its Common Stock under the Securities Act, if any (the “IPO”), your target annual incentive bonus opportunity shall be 35% of your annualized base salary.

Equity Grant. Any existing grants of equity you have in the Company will be treated consistent with the terms of the applicable agreements under which such awards have been granted. You may be awarded additional equity grants from time to time in accordance with normal business practice and in the sole discretion of the Company’s Board of Directors. The terms of any future equity grant will be consistent with any plan under which they are granted and the terms of the applicable agreement for the award(s).

Benefits. You may participate in any and all benefit programs that the Company establishes and makes available to its employees from time to time, subject to the terms and conditions of those programs. The Company’s benefits programs are subject to change at any time in the Company’s sole discretion.

Vacation. You will be entitled to annual paid vacation of four (4) weeks. Your accrual and use of vacation time will be pursuant to any vacation or time off policy the Company may establish or modify from time to time. The Company’s vacation policy is subject to change at any time in the Company’s sole discretion.

Severance. If the Company terminates your employment without Cause (as defined below) or you resign your employment with the Company for Good Reason (as defined below) (in either event, a “Qualifying Termination”), then, subject to your execution of a reasonable release acceptable to the Company (the “Release”), the expiration of any revocation period provided in the Release and your continued compliance with the terms of the NDA (as defined below), the Company will pay you an amount (the “Regular Severance Amount”) equal to your then-current base salary rate for a period of six (6) months, provided that, if any such Qualifying Termination occurs at any time after the IPO, if any, the Regular Severance Amount shall be an amount equal to your then-current base salary rate for a period of nine (9) months.

If there is a Qualifying Termination within the three (3) months immediately preceding or the twelve (12) months immediately following a Change of Control (as defined in the Company’s 2015 Equity Incentive Plan, as may be amended and in effect from time to time or succeeded or superseded by a successor equity incentive plan), then, subject to your execution of a Release following your Separation from Service (as defined below), the expiration of any revocation period provided in the Release and your continued compliance with the terms of the NDA, the Company will pay you, in lieu of any Regular Severance Amount, an amount (the “Change of Control Severance Amount”) equal to your then-current base salary rate for a period of twelve (12) months plus an amount equal to 100% of your then-applicable target annual incentive bonus.

Any severance amount to which you may be entitled under this letter will be paid in substantially equal installments in accordance with the Company’s ordinary payroll practices, beginning on the first payroll date following the date that is either (i) sixty (60) days after the date of your Separation from Service or (ii) in the case of a Separation from Service that is a Qualifying Termination that occurs within three (3) months immediately preceding a Change of

Control, sixty (60) days after such Change of Control, provided that, in the case of either of the foregoing clauses (i) and (ii), the Company, in its sole discretion, may have the option to pay any such severance amount to you as a lump sum. To be eligible for either the Regular Severance Amount or the Change of Control Severance Amount, as applicable, you must execute and deliver the Release to the Company and allow it to become effective within thirty (30) days of your Separation from Service or, if later, within thirty (30) days of a Change of Control giving rise to a Change of Control Severance Amount entitlement.

In addition, if following your Separation from Service, you are eligible for and timely elect continued medical insurance coverage pursuant to COBRA, the Company will reimburse you for the applicable premiums for you and your eligible dependents during the period commencing on the date of your Separation from Service and ending on the earlier to occur of (a) the final day of the applicable severance period and (b) the date you otherwise become ineligible for continued coverage under COBRA. Notwithstanding the foregoing, if the Company determines that it cannot provide such reimbursement of premiums to you without potentially violating applicable law, the Company shall not be obligated to make any such payments or reimbursements to you.

If the Qualifying Termination occurs within the three (3) months immediately preceding or the twelve (12) months immediately following a Change of Control, then each outstanding equity award in the Company held by you shall immediately vest and, if applicable, become exercisable with respect to one hundred percent (100%) of the shares of equity of the Company subject thereto. The foregoing provisions of this paragraph shall apply notwithstanding anything express or implied to the contrary in any agreement or award between you and the Company, or in any plan of the Company, that is applicable to such outstanding equity award.

Notwithstanding anything herein to the contrary, in the event that any compensation or benefit that constitutes “nonqualified deferred compensation” within the meaning of Section 409A of the Internal Revenue Code of 1986, as amended (the “Code”), becomes payable upon the occurrence of a Change of Control, such compensation or benefit shall not be paid unless such Change of Control constitutes a “change in control event” within the meaning of Section 409A of the Code.

If any payment or benefit you would receive under this letter, when combined with any other payment or benefit you receive pursuant to the termination of your employment with the Company (“Payment”) would (i) constitute a “parachute payment” within the meaning of Section 280G of the Code, and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the “Excise Tax”), then such Payment shall be either (x) the full amount of such Payment or (y) such lesser amount (with your choice of whether to reduce cash payments or stock option compensation or both) as would result in no portion of the Payment being subject to the Excise Tax, whichever of the foregoing amounts, taking into account the applicable federal, state and local employment taxes, income taxes and the Excise Tax results in your receipt, on an after-tax basis, of the greater amount of the Payment notwithstanding that all or some portion of the Payment may be subject to the Excise Tax.

Definitions

Separation from Service. For purposes of this letter, “Separation from Service” means a “separation from service” within the meaning of Section 409A of the Code. Each installment payment provided under this letter shall at all times be considered a separate and distinct payment for purposes of Section 409A of the Code. Notwithstanding anything in this letter to the contrary, to the extent required to avoid a prohibited distribution under Section 409A of the Code, the benefits provided under this letter will not be provided to you until the earlier of (a) the expiration of the six-month period measured from the date of your Separation from Service with the Company or (b) the date of your death. Upon the first business day after expiration of the relevant period, all payments delayed pursuant to the preceding sentence will be paid in a lump sum and any remaining payments due will be paid as otherwise provided herein.

Cause. “Cause” shall mean the occurrence of any of the following events by the individual: (i) commission of any crime involving the Company, or any crime involving fraud, breach of trust, or physical or emotional harm to any person, moral turpitude or dishonesty; (ii) any unauthorized use or disclosure of the Company’s proprietary information (other than any such use or disclosure that is not intentional and is not material); (iii) any intentional misconduct or gross negligence that has a material adverse effect on the Company’s business or reputation; (iv) any material breach by you of any agreement between you and the Company that is not cured within thirty (30) days after receipt of written notice from the Company describing any such breach; or (v) repeated and willful failure to perform the duties, functions and responsibilities of the individual’s position after a written warning from the Company.

Good Reason. “Good Reason” shall mean your resignation from all positions you then hold with the Company if: (A) without your written consent (i) there is a material diminution in the nature or scope of your responsibilities, duties, authority, or title; (ii) there is a material reduction of your base salary; provided, however, that a material reduction in your base salary pursuant to a salary reduction program affecting all or substantially all of the employees of the Company and that does not adversely affect you to a greater extent than other similarly situated employees shall not constitute Good Reason; or (iii) you are required to relocate your primary work location to a facility or location that would increase your one way commute distance by more than thirty-five (35) miles from your primary work location as of immediately prior to such change, (B) you provide written notice outlining such conditions, acts or omissions to the Company’s Chief Executive Officer, President, Chief Financial Officer or General Counsel within thirty (30) days immediately following such material change or reduction, (C) such material change or reduction is not remedied by the Company within thirty (30) days following the Company’s receipt of such written notice and (D) your resignation is effective not later than thirty (30) days after the expiration of such thirty (30) day cure period. “Good Reason” shall also mean your resignation on the one year anniversary of a Change of Control from all positions you then hold with the Company or its successor if by that date you have not entered into a written letter or agreement with the Company or such successor that provides for your continued employment with the Company or such successor. For purposes of clarification, any Qualifying Termination that occurs on the first anniversary of a Change of Control shall be deemed and treated as occurring within the twelve (12) months immediately following a Change of Control for all purposes of this letter.

Invention, Non-Disclosure, Non-Competition and Non-Solicitation Obligations. You previously have executed and delivered the Company’s standard form of Employee Proprietary Information, Inventions, Non-Competition and Non-Solicitation Agreement (the “NDA”), an executed copy of which is attached hereto as Exhibit A.

At-Will Employment. This letter shall not be construed as an agreement, either express or implied, to employ you for any stated term, and shall in no way alter the Company’s policy of employment at-will. Similarly, nothing in this letter shall be construed as an agreement, either express or implied, to pay you any compensation or grant you any benefit beyond the end of your employment with the Company, except as otherwise explicitly set forth in this letter. This

letter supersedes all prior understandings, whether written or oral, including, without limitation, your current employment agreement, with respect to the subject matter of this letter.

[The remainder of this page is intentionally left blank.]

Please indicate your acceptance of this letter agreement by signing below in the space provided for your signature.

Sincerely,

/s/ Keith M. Gottesdiener

Keith M. Gottesdiener
Chief Executive Officer

The foregoing correctly sets forth the terms of my at-will employment with the Company. I am not relying on any representations other than those set forth above.

/s/ Fred Fiedorek

September 13, 2017

Fred Fiedorek

Date



EXHIBIT A

EXECUTED NDA

[See attached]

RHYTHM PHARMACEUTICALS, INC.

**EMPLOYEE PROPRIETARY INFORMATION, INVENTIONS, NON-COMPETITION
AND NON-SOLICITATION AGREEMENT**

In consideration and as a condition of my employment, or continued employment, by Rhythm Pharmaceuticals, Inc., a Delaware corporation (the "Company"), and the compensation now and hereafter paid to me, I hereby agree as follows:

1. NONDISCLOSURE

1.1 Recognition of Company's Rights; Nondisclosure. At all times during my employment by the Company and thereafter, I will hold in strictest confidence and will not disclose, use, lecture upon, or publish any of the Company's Proprietary Information (defined below), except as such disclosure, use, lecture, or publication may be required in connection with my work for the Company, or unless any other individual that is an officer of the Company expressly authorizes such in writing. I will obtain the Company's prior written approval before publishing or submitting for publication any material (written, oral, or otherwise) that relates to my work at the Company or incorporates any Proprietary Information. Notwithstanding the foregoing, disclosure of any such Proprietary Information shall not be prohibited if such disclosure is directly related to a valid and existing order of a court or other governmental body or agency; *provided, however,* that I shall have first given prompt notice to the Company of any possible or prospective order and the Company shall have been afforded a reasonable opportunity to prevent or limit any such disclosure. I hereby assign to the Company any rights I may have or acquire in any Proprietary Information and recognize that all Proprietary Information shall be the sole property of the Company and its assigns.

1.2 Proprietary Information. The term "Proprietary Information" means any and all confidential or proprietary knowledge, data or information of the Company or any of its subsidiaries or controlled affiliates. By way of illustration but not limitation, "Proprietary Information" includes: (a) developments, inventions, ideas, data, programs, other works of authorship, designs and techniques, trade secrets, mask works, processes, formulas, source and object codes, algorithms, compositions of matter, chemical structures, formulations, methods (including, without limitation, methods of use, delivery or manufacture), dosing regimens, know-how, technology, improvements and discoveries (hereinafter collectively referred to as "Inventions"); (b) the design of, and all other information with respect to, preclinical studies and clinical trials, including, without limitation, the results of such preclinical studies and clinical trials; (c) clinical development and regulatory approval strategy; (d) information regarding research collaborations, joint development relationships, licensing relationships and transactions, corporate partnering relationships and transactions, joint ventures and other strategic alliances, including, without limitation, the research, development and commercialization activities, areas or fields subject to such relationships or transactions, the results of such research, development or commercialization activities and the terms of any agreements entered into by the Company or any of its subsidiaries or controlled affiliates in connection with such relationships or transactions; (e) information regarding plans for research, development, new services or products, marketing and selling, business plans, budgets and unpublished financial statements, licenses, prices and costs, clients, customers, and suppliers; and (f) information regarding the skills and compensation of the employees and/or consultants of the Company or any of its

subsidiaries or controlled affiliates. For purposes of this Employee Proprietary Information, Inventions, Non-Competition and Non-Solicitation Agreement (this “Agreement”), the term “Proprietary Information” shall not include information which is or becomes publicly available without breach of: (i) this Agreement; (ii) any other agreement or instrument to which the Company or any of its subsidiaries or controlled affiliates is a party or a beneficiary; or (iii) any duty owed to the Company or any of its subsidiaries or controlled affiliates by me or by any third party; *provided, however*, that if I shall seek to disclose, use, lecture upon, or publish any Proprietary Information, I shall bear the burden of proving that any such information shall have become publicly available without any such breach.

1.3 Third Party Information. I understand that the Company or any of its subsidiaries or controlled affiliates has received and in the future will receive from third parties confidential or proprietary information (“Third Party Information”) subject to a duty to maintain the confidentiality of such information and to use it only for certain limited purposes. During the term of my employment by the Company and thereafter, I will hold Third Party Information in the strictest confidence and will not disclose Third Party Information to anyone (other than personnel of the Company or any of its subsidiaries or controlled affiliates who need to know such information in connection with their work for the Company or any of its subsidiaries or controlled affiliates) and will not use Third Party Information (except in connection with my work for the Company or any of its subsidiaries or controlled affiliates), unless and to the extent that any other individual that is an officer of the Company expressly authorizes such disclosure or use in writing. I hereby assign to the Company any rights I may have or acquire in any Third Party Proprietary Information during my employment with the Company.

1.4 No Improper Use of Information of Prior Employers and Others. During my employment by the Company, I will not improperly use or disclose any confidential information or trade secrets, if any, of any former employer or any other person to whom I have an obligation of confidentiality, and I will not bring onto the premises of the Company or any of its subsidiaries or controlled affiliates any unpublished documents or any property belonging to any former employer or any other person to whom I have an obligation of confidentiality unless consented to in writing by that former employer or person. I will use in the performance of my duties only information which is generally known and used by persons with training and experience comparable to my own, which is common knowledge in the industry or otherwise legally in the public domain, or which is otherwise provided or developed by, or on behalf of, the Company or any of its subsidiaries or controlled affiliates.

1.5 Defend Trade Secrets Act. Pursuant to 18 U.S.C. § 1833(b), I will not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of a trade secret of the Company or its affiliates that (a) I make (i) in confidence to a Federal, State, or local government official, either directly or indirectly, or to my attorney and (ii) solely for the purpose of reporting or investigating a suspected violation of law; or (b) I make in a complaint or other document that is filed under seal in a lawsuit or other proceeding. If I file a lawsuit for retaliation by the Company for reporting a suspected violation of law, I may disclose the trade secret to my attorney and use the trade secret information in the court proceeding, if I (x) file any document containing the trade secret under seal, and (y) do not disclose the trade secret, except pursuant to court order. Nothing in this Agreement is intended to conflict with 18 U.S.C. § 1833(b) or create liability for disclosures of trade secrets that are expressly allowed by 18 U.S.C. § 1833(b).

2. ASSIGNMENT OF INVENTIONS

2.1 Proprietary Rights. The term “Proprietary Rights” means all trade secret, patent, copyright, mask work and other intellectual property rights throughout the world.

2.2 Prior Inventions. Inventions, if any, patented or unpatented, which I made prior to the commencement of my employment with the Company are excluded from the scope of this Agreement. To preclude any possible uncertainty, I have set forth on Exhibit A (Prior Inventions) attached hereto a complete list of all Inventions that I have, alone or jointly with others, conceived, developed or reduced to practice or caused to be conceived, developed or reduced to practice prior to the commencement of my employment with the Company, that I consider to be my property or the property of third parties and that I wish to have excluded from the scope of this Agreement (collectively referred to as “Prior Inventions”). If disclosure of any such Prior Invention would cause me to violate any prior confidentiality agreement, I understand that I am not to list such Prior Inventions in Exhibit A but am only to disclose a cursory name for each such invention, a listing of the party or parties to whom it belongs, and the fact that full disclosure as to such inventions has not been made for that reason. A space is provided on Exhibit A for such purpose. If I do not attach such disclosure, I am representing thereby that there are no Prior Inventions. If, in the course of my employment with the Company, I incorporate a Prior Invention (whether or not such Prior Invention is listed in Exhibit A) into a product, compound, composition of matter, chemical structure, biological material, formulation, method, process or machine of the Company or any of its subsidiaries or controlled affiliates, or I in any way otherwise use, or make available for use, a Prior Invention (whether or not such Prior Invention is listed in Exhibit A) in connection with the research, development, manufacture, use or commercialization of any such product, compound, composition of matter, chemical structure, biological material, formulation, method, process or machine, the Company is hereby granted and shall have a nonexclusive, royalty free, irrevocable, perpetual, worldwide license (with rights to sublicense through multiple tiers of sublicensees) to research, cause to be researched, develop, cause to be developed, make, cause to be made, modify, cause to be modified, use, cause to be used and sell or otherwise commercialize, or cause to be sold or otherwise commercialized, such Prior Invention. Notwithstanding the foregoing, I agree that I will not incorporate, or permit to be incorporated, Prior Inventions in any Company Inventions (as defined in Section 2.3 below), or in any product, compound, composition of matter, chemical structure, biological material, formulation, method, process or machine of the Company or any of its subsidiaries or controlled affiliates, without the Company’s prior written consent.

2.3 Assignment of Inventions. Subject to this Section 2.3 and to Sections 2.5 and 2.6, I hereby assign to the Company all my right, title and interest in and to any and all Inventions (and all Proprietary Rights with respect thereto), whether or not patentable or registrable under copyright or similar statutes, that are made, conceived, reduced to practice or learned by me, either alone or jointly with others, (i) in the course of my employment with the Company, (ii) during the term of my employment with the Company (whether or not in the course of my employment with the Company and whether or not during regular business hours) if and to the extent that any such Invention relates to the actual business or planned business of the Company or was made, conceived or reduced to practice by me, either alone or jointly with others, as a result of any material use of any of the properties, assets or facilities of the Company or (iii) arising out of, based upon, or resulting from the use of, any Proprietary Information or Third-Party Proprietary Information made available to me or to which I had access as an

employee of the Company. Inventions assigned pursuant to this Section 2 to the Company, or to a third party as directed by the Company pursuant to Section 2.5 below, are hereinafter referred to as "Company Inventions." At the request of the Company at any time and from time to time, I will execute and deliver any and all instruments, documents and agreements reasonably requested by the Company for purposes of confirming my assignment to the Company of all of my right, title and interest in and to any and all Company Inventions (and all Proprietary Rights with respect thereto), including, without limitation, at any time when any such Company Inventions (or any Proprietary Rights with respect thereto) are first reduced to practice or first fixed in a tangible medium, as applicable.

For the avoidance of doubt, notwithstanding any contrary provision contained herein, nothing contained in this Agreement shall require the assignment of any Invention (or Proprietary Right with respect thereto) made or conceived by me during the period of my employment to the extent such assignment is prohibited by any applicable state or federal law.

2.4 Obligation to Keep Company Informed. During the period of my employment with the Company and thereafter, I will promptly disclose to the Company fully and in writing all Company Inventions authored, conceived or reduced to practice by me, either alone or jointly with others. In addition, during the period of my employment with the Company and thereafter, I will promptly disclose to the Company all patent applications filed by me or on my behalf that claim any Company Invention.

2.5 Government or Third Party. I also agree to assign all my right, title and interest in and to any particular Company Invention to a third party, including without limitation the United States, as directed by the Company.

2.6 Works for Hire. I acknowledge that all original works of authorship which are made by me (solely or jointly with others) within the scope of my employment with the Company and which are protectable by copyright are "works made for hire," pursuant to the United States Copyright Act (17 U.S.C., Section 101).

2.7 Enforcement of Proprietary Rights. I will assist the Company in every proper way in obtaining, and from time to time enforcing, United States and foreign Proprietary Rights relating to Company Inventions in any and all countries. To that end I will promptly execute, verify and deliver such documents and perform such other acts (including appearances as a witness) as the Company may reasonably request for use in applying for, obtaining, perfecting, evidencing, sustaining and enforcing such Proprietary Rights and the assignment thereof. In addition, I will promptly execute, verify and deliver assignments of such Proprietary Rights to the Company or its designee. My obligation to assist the Company with respect to Proprietary Rights relating to such Company Inventions in any and all countries shall continue beyond the termination of my employment with the Company, but the Company shall compensate me at a reasonable rate after my termination for the time actually spent by me at the Company's request on such assistance.

In the event the Company is unable for any reason, after reasonable effort, to secure my signature on any document needed in connection with the actions specified in the preceding paragraph, I hereby irrevocably designate and appoint the Company and its duly authorized officers and agents as my agents and attorneys-in-fact, subject to full power or substitution and resubstitution, which appointment is coupled with an interest, to act for and in my behalf to execute, verify and

file any such documents and to do all other lawfully permitted acts to further the purposes of the preceding paragraph with the same legal force and effect as if executed by me. I hereby waive and quitclaim to the Company any and all claims, of any nature whatsoever, which I now or may hereafter have for infringement of any Proprietary Rights assigned hereunder to the Company.

3. RECORDS. I agree to keep and maintain adequate and current records (in the form of notes, memoranda, sketches, drawings and in any other form that may be required by the Company) of all Proprietary Information and all Company Inventions made, conceived, developed or reduced to practice by me, which records shall be available to and remain the sole property of the Company at all times.

4. NON-SOLICITATION. I agree that, during the period of my employment with the Company and for the one **(1)** year period after the date my employment with the Company ends for any reason, including but not limited to voluntary termination by me or termination by the Company, I will not, for myself or for the benefit of any other person (including, without limitation, any other person with which I may have a direct or indirect interest or relationship as an employee, consultant, advisor, equityholder or otherwise): (a) solicit, hire or engage, or attempt to solicit, hire or engage, any individual as an employee, consultant, advisor, officer, manager, managing partner, director or in any other similar capacity if such individual shall have been an employee of the Company or any of its subsidiaries or controlled affiliates at any time during the one (1) year period prior to the date of termination of my employment with the Company; (b) solicit, induce or attempt to induce any customer, vendor, contractor, consultant or advisor of the Company or any of its subsidiaries or controlled affiliates to terminate, diminish, or materially alter his, her or its relationship with the Company or any of its subsidiaries or controlled affiliates; or (c) solicit, induce or attempt to induce any potential customer, vendor, contractor, employee, consultant or advisor whose identity and potential relationship with the Company or any of its subsidiaries or controlled affiliates I learned as a result of my employment with the Company, not to establish, or to diminish or materially alter, such potential relationship with the Company or any of its subsidiaries or controlled affiliates. In the event that a court finds this Section 4, or any of its restrictions, to be unenforceable or invalid, I and the Company agree that (i) this Section 4 will be automatically modified to provide the Company with the maximum protection of its business interests allowed by law and (ii) I shall be bound, and such court shall enforce, this Section 4 as so modified.

5. NON-COMPETITION. I agree that, during the term of my employment with the Company and for the one **(1)** year period after the date my employment with the Company ends for any reason, including but not limited to voluntary termination by me or termination by the Company, I will not, directly or indirectly, as an officer, director, manager, employee, consultant, advisor, owner, partner, member, stockholder, or in any other capacity, (a) compete with the business or planned business of the Company or any of its subsidiaries or controlled affiliates, or (b) take any steps or actions to facilitate or prepare for competition with the business or planned business of the Company or any of its subsidiaries or controlled affiliates, nor will I assist another person to take any action that I would be prohibited from taking under this Section 5. The obligations not to compete that I have undertaken under this Section 5 shall apply in all countries of the world. For purposes of this Section 5, I will not be deemed or treated as being in competition with the business or planned business of the Company or any of its subsidiaries or controlled affiliates or as being in violation of the covenant set forth in the clause (b) above in this Section 5 merely by virtue of my ownership of any equity interest in any business or person that is in

competition with, or is planning to be in competition with, the business or planned business of the Company or any of its subsidiaries or controlled affiliates, if my ownership of any such equity interest represents five percent (5%) or less the total equity interests in such business or person. I hereby acknowledge and agree that the foregoing restrictions contained in this Section 5 are reasonable, proper and necessitated by the legitimate business interests of the Company and will not prevent me from earning a living or pursuing my career. In the event that a court finds this Section 5, or any of its restrictions, to be unenforceable or invalid, I and the Company agree that (i) this Section 5 will be automatically modified to provide the Company with the maximum protection of its business interests allowed by law and (ii) I shall be bound, and such court shall enforce, this Section 5 as so modified.

6. NO CONFLICTING OBLIGATION. I represent that my performance of all the terms of this Agreement and as an employee of the Company has not breached, and does not and will not breach, any agreement to keep in confidence information acquired by me in confidence or in trust prior to, or outside the scope of, my employment by the Company and any agreement not to compete with the business of any third party. I have not entered into, and I agree I will not enter into, any agreement, either written or oral, in conflict herewith.

7. RETURN OF COMPANY DOCUMENTS. When I leave the employ of the Company, I will deliver to the Company any and all notes, memoranda, specifications, drawings, devices, formulas, and documents, together with all copies thereof, and any other material containing or disclosing any Company Inventions, Third Party Information or Proprietary Information of the Company. I further agree that, during the term of my employment with the Company or at any time thereafter, any property situated on the premises of the Company or any of its subsidiaries or controlled affiliates, including disks and other storage media, filing cabinets or other work areas, is subject to inspection by Company personnel at any time with or without notice. In the event I leave the employ of the Company for any reason whatsoever, I will promptly sign and deliver the "Termination Certificate" attached hereto as Exhibit B.

8. LEGAL AND EQUITABLE REMEDIES. Because my services are personal and unique and because I may have access to and become acquainted with the Proprietary Information of the Company, the Company shall have the right to enforce this Agreement and any of its provisions by injunction, specific performance, or other equitable relief, without bond and without prejudice to any other rights and remedies that the Company may have for a breach of this Agreement. In the event that the Company enforces the provisions of Section 4 or Section 5 hereof through a court order, I agree that the restrictions contained in Section 4 or Section 5, as the case may be, shall remain in effect for a period of one year from the effective date of such court order. I agree that if the Company is successful in whole or in part in any legal or equitable action against me under this Agreement, the Company shall be entitled to recover from me all costs, including reasonable attorney's fees, incurred by the Company in connection with such legal or equitable action.

9. NOTICES. Any notices required or permitted hereunder shall be given to the appropriate party at the address specified below or at such other address as the party shall specify in writing. Such notice shall be deemed given upon personal delivery to the appropriate address, one (1) business day after dispatch if sent by nationally recognized courier or overnight delivery service, on the date of dispatch if sent by facsimile or electronic mail for which confirmation of

transmission is provided or, if sent by certified or registered mail, three (3) business days after the date of mailing.

10. NOTIFICATION OF NEW EMPLOYER. In the event that I leave the employ of the Company and accept new employment, I hereby agree to notify my new employer of my rights and obligations under this Agreement and I hereby consent to the Company or any person on behalf of the Company providing notice to my new employer of such rights and obligations.

11. GENERAL PROVISIONS

11.1 Governing Law; Consent to Personal Jurisdiction. This Agreement will be governed by and construed according to the laws of the Commonwealth of Massachusetts, as such laws are applied to agreements entered into and to be performed entirely within Massachusetts between Massachusetts residents. I hereby expressly consent to the personal jurisdiction of the state and federal courts located in the Commonwealth of Massachusetts for any lawsuit filed there against me by the Company arising from or related to this Agreement.

11.2 Severability. In case any one or more of the provisions contained in this Agreement shall, for any reason, be held to be invalid, illegal, or unenforceable in any respect, such invalidity, illegality, or unenforceability shall not affect the other provisions of this Agreement, and this Agreement shall be construed as if such invalid, illegal, or unenforceable provision had never been contained herein. Moreover, if any one or more of the provisions contained in this Agreement shall for any reason be held to be excessively broad as to duration, geographical scope, activity or subject, it shall be construed by limiting and reducing it, so as to be enforceable to the extent compatible with the applicable law as it shall then appear.

11.3 Successors and Assigns. This Agreement will be binding upon my heirs, executors, administrators and other legal representatives and will be for the benefit of the Company, its successors, and its assigns. Without limiting the generality of the foregoing, if I become an employee of any subsidiary or controlled affiliate of the Company, then (i) such subsidiary or controlled affiliate shall be deemed and treated as an intended third party beneficiary of this Agreement to the same extent as if such subsidiary or controlled affiliate were a party to this Agreement and (ii) each reference in this Agreement to the term "Company" shall be deemed to be a reference to whichever of Rhythm Pharmaceuticals, Inc. and/or such subsidiary, parent or controlled affiliate is my employer.

11.4 Survival. The provisions of this Agreement shall survive the termination of my employment with the Company and the assignment of this Agreement by the Company to any successor in interest or other assignee.

11.5 Employment. I agree and understand that nothing in this Agreement shall confer any right with respect to continuation of my employment by the Company, nor shall it interfere in any way with my right or the Company's right to terminate my employment at any time, with or without cause.

11.6 Waiver. No waiver by the Company of any breach of this Agreement shall be a waiver of any preceding or succeeding breach. No waiver by the Company of any right under this Agreement shall be construed as a waiver of any other right. The Company shall not be required to give notice to enforce strict adherence to all terms of this Agreement.

11.7 Entire Agreement. My obligations, and the Company's rights, under this Agreement shall apply to any time during which I was previously employed, or am in the future employed, by the Company. This Agreement is the final, complete and exclusive agreement of the parties with respect to the subject matter hereof and supersedes all prior agreements relating to the subject matter hereof and merges all prior discussions between us. No modification of or amendment to this Agreement, nor any waiver of any rights under this Agreement, will be effective unless in writing and signed by the party to be charged. Any subsequent change or changes in my duties, salary or compensation will not affect the validity or scope of this Agreement.

11.8 Counterparts. This Agreement may be signed in counterparts, each shall be deemed an original and shall together constitute one agreement.

11.9 Acknowledgement. I acknowledge that this Agreement is a condition to my employment with the Company and that I have had a full and adequate opportunity to read, understand and discuss with my advisors, including legal counsel, the terms and conditions contained in this Agreement prior to signing hereunder.

This Agreement shall be effective as of the first day of my employment with the Company.

[Remainder of page intentionally left blank]

I HAVE READ THIS AGREEMENT CAREFULLY AND UNDERSTAND ITS TERMS. I HAVE COMPLETELY FILLED OUT EXHIBIT A TO THIS AGREEMENT.

Dated: 11/16/16

/s/ Fred T. Fiedorek

Name: Fred T. Fiedorek

Address:

ACCEPTED AND AGREED:

RHYTHM PHARMACEUTICALS, INC.

By: /s/ Bart Henderson

Name: Bart Henderson

Title: President

Dated: 11/16/16

EXHIBIT A

TO: Rhythm Pharmaceuticals, Inc.

FROM:

DATE:

SUBJECT: Prior Inventions

1. Except as listed in Section 2 below, the following is a complete list of all inventions or improvements relevant to the subject matter of my employment by Rhythm Pharmaceuticals, Inc. (the "Company") that have been made or conceived or first reduced to practice by me alone or jointly with others prior to my employment by the Company:
 - o No inventions or improvements.
 - o See below:
 - o Additional sheets attached.
2. Due to a prior confidentiality agreement, I cannot complete the disclosure under Section 1 above with respect to inventions or improvements generally listed below, the proprietary rights and duty of confidentiality with respect to which I owe to the following party(ies):

Invention or Improvement	Party(ies)	Relationship
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1.

2.

3.

o Additional sheets attached.

3. I acknowledge that this *Exhibit A*, if completed, forms a part of the Employee Proprietary Information, Inventions, Non-Competition and Non-Solicitation Agreement to which the Company and I are parties and that the failure to complete this *Exhibit A* and cause it to be attached to such Agreement constitutes a representation by me that I have no Prior Inventions.
-

EXHIBIT B

TERMINATION CERTIFICATE

I hereby confirm and certify to the Company that I have returned to the Company all Proprietary Information in my possession or control, that I have disclosed fully to the Company all Company Inventions and that I have and will comply fully with all of my obligations to the Company under my Employee Proprietary Information, Inventions, Non-Competition and Non-Solicitation Agreement with the Company.

Name:



Rhythm Pharmaceuticals, Inc.
500 Boylston Street — 11th Floor
Boston, MA 02116
Main Telephone: 617-585-2090
www.rhythmtx.com

September 13, 2017

Hunter Smith
c/o Rhythm Pharmaceuticals, Inc.
500 Boylston Street, 11th Floor
Boston, MA 02116

Dear Hunter:

On behalf of Rhythm Pharmaceuticals, Inc., formerly known as Rhythm Metabolic, Inc. (the “Company” or “Rhythm”), I am pleased to set forth below the amended and restated terms of your employment with the Company.

Employment. You are currently the Chief Financial Officer of the Company, and during the term of your employment with the Company, you will continue to hold the position and title of Chief Financial Officer. During the term of your employment with the Company, you will be responsible for performing the duties associated with the position above or as the Company may otherwise assign to you. Your primary place of employment initially will be in the Company’s offices located in Boston, Massachusetts; however, you will be expected to travel as may be necessary to fulfill your responsibilities. In the course of your employment with the Company, you will be subject to, and required to comply with, all Company policies and all applicable laws and regulations.

Base Salary. During your employment, your salary will be \$380,000 annualized, subject to all required and elected taxes and other withholdings. Your salary may be adjusted from time to time in accordance with normal business practice and in the sole discretion of the Company.

Annual Incentive Bonus. Following the end of each fiscal year and subject to the approval by the Company’s Board of Directors, you will be eligible to earn an incentive bonus, based on your performance and the Company’s performance, each during the applicable fiscal year, if your employment continues in good standing on the date of payment of such incentive bonus. Your target annual incentive bonus opportunity shall be 30% of your annualized base salary, provided that, from and after the closing of the Company’s first underwritten public offering of its Common Stock under the Securities Act, if any (the “IPO”), your target annual incentive bonus opportunity shall be 35% of your annualized base salary.

Equity Grant. Any existing grants of equity you have in the Company will be treated consistent with the terms of the applicable agreements under which such awards have been granted. You may be awarded additional equity grants from time to time in accordance with normal business practice and in the sole discretion of the Company’s Board of Directors. The terms of any future equity grant will be consistent with any plan under which they are granted and the terms of the applicable agreement for the award(s).

Sign-on Bonus and Travel and Relocation Expenses. Rhythm will agree to reimburse you for up to \$125,000 in travel, commuting, lodging and other expenses (including moving your family to Boston if you decide to do so), and for appropriate relocation expenses. On the second anniversary of July 31, 2017 (i.e., July 31, 2019), which will represent the end of two years of employment, if less than \$125,000 has been expensed for these purposes, Rhythm will provide the balance to you in the form of a cash sign-on bonus.

Benefits. You may participate in any and all benefit programs that the Company establishes and makes available to its employees from time to time, subject to the terms and conditions of those programs. The Company’s benefits programs are subject to change at any time in the Company’s sole discretion.

Vacation. You will be entitled to annual paid vacation of four (4) weeks. Your accrual and use of vacation time will be pursuant to any vacation or time off policy the Company may establish or modify from time to time. The Company’s vacation policy is subject to change at any time in the Company’s sole discretion.

Outside Board Duties. You currently serve as an independent director of the NYSE listed multinational Genessee & Wyoming Inc. (“Genessee”), and as a member of its Governance/Nominating Committee. You may remain as a director of Genessee, provided that your duties in such director role shall not in any way interfere with your role and duties as Chief Financial Officer of, and commitments to, the Company which shall supersede and take priority in any and all respects. Moreover, you agree that you will not be permitted to take on any additional director, board observer, advisory, consulting, or other such roles or commitments without the express prior written consent of the Chief Executive Officer of the Company.

Severance. If the Company terminates your employment without Cause (as defined below) or you resign your employment with the Company for Good Reason (as defined below) (in either event, a “Qualifying Termination”), then, subject to your execution of a reasonable release acceptable to the Company (the “Release”), the expiration of any revocation period provided in the Release and your continued compliance with the terms of the NDA (as defined below), the Company will pay you an amount (the “Regular Severance Amount”) equal to your then-current base salary rate for a period of six (6) months, provided that, (i) if any such Qualifying Termination occurs at any time after the IPO, if any, the Regular Severance Amount shall be an amount equal to your then-current base salary rate for a period of nine (9) months and (ii) if any such Qualifying Termination occurs on, or at any time prior to, the first anniversary

of the start date of your employment with the Company (even if such first anniversary occurs after the IPO), the Regular Severance Amount shall be an amount equal to your then-current base salary rate for a period of twelve (12) months.

If there is a Qualifying Termination within the three (3) months immediately preceding or the twelve (12) months immediately following a Change of Control (as defined in the Company's 2015 Equity Incentive Plan, as may be amended and in effect from time to time or succeeded or superseded by a successor

equity incentive plan), then, subject to your execution of a Release following your Separation from Service (as defined below), the expiration of any revocation period provided in the Release and your continued compliance with the terms of the NDA, the Company will pay you in lieu of any Regular Severance Amount, an amount (the "Change of Control Severance Amount") equal to your then-current base salary rate for a period of twelve (12) months plus an amount equal to 100% of your then-applicable target annual incentive bonus.

Any severance amount to which you may be entitled under this letter will be paid in substantially equal installments in accordance with the Company's ordinary payroll practices, beginning on the first payroll date following the date that is either (i) sixty (60) days after the date of your Separation from Service or (ii) in the case of a Separation from Service that is a Qualifying Termination that occurs within three (3) months immediately preceding a Change of Control, sixty (60) days after such Change of Control, provided that, in the case of either of the foregoing clauses (i) and (ii), the Company, in its sole discretion, may have the option to pay any such severance amount to you as a lump sum. To be eligible for either the Regular Severance Amount or the Change of Control Severance Amount, as applicable, you must execute and deliver the Release to the Company and allow it to become effective within thirty (30) days of your Separation from Service or, if later, within thirty (30) days of a Change of Control giving rise to a Change of Control Severance Amount entitlement.

In addition, if following your Separation from Service, you are eligible for and timely elect continued medical insurance coverage pursuant to COBRA, the Company will reimburse you for the applicable premiums for you and your eligible dependents during the period commencing on the date of your Separation from Service and ending on the earlier to occur of (a) the final day of the applicable severance period and (b) the date you otherwise become ineligible for continued coverage under COBRA. Notwithstanding the foregoing, if the Company determines that it cannot provide such reimbursement of premiums to you without potentially violating applicable law, the Company shall not be obligated to make any such payments or reimbursements to you.

If the Qualifying Termination occurs within the three (3) months immediately preceding or the twelve (12) months immediately following a Change of Control, then each outstanding equity award in the Company held by you shall immediately vest and, if applicable, become exercisable with respect to one hundred percent (100%) of the shares of equity of the Company subject thereto. The foregoing provisions of this paragraph shall apply notwithstanding anything express or implied to the contrary in any agreement or award between you and the Company, or in any plan of the Company, that is applicable to such outstanding equity award.

Notwithstanding anything herein to the contrary, in the event that any compensation or benefit that constitutes "nonqualified deferred compensation" within the meaning of Section 409A of the Internal Revenue Code of 1986, as amended (the "Code"), becomes payable upon the occurrence of a Change of Control, such compensation or benefit shall not be paid unless such Change of Control constitutes a "change in control event" within the meaning of Section 409A of the Code.

If any payment or benefit you would receive under this letter, when combined with any other payment or benefit you receive pursuant to the termination of your employment with the Company ("Payment") would (i) constitute a "parachute payment" within the meaning of Section 280G of the Code, and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax"),

then such Payment shall be either (x) the full amount of such Payment or (y) such lesser amount (with your choice of whether to reduce cash payments or stock option compensation or both) as would result in no portion of the Payment being subject to the Excise Tax, whichever of the foregoing amounts, taking into account the applicable federal, state and local employment taxes, income taxes and the Excise Tax results in your receipt, on an after-tax basis, of the greater amount of the Payment notwithstanding that all or some portion of the Payment may be subject to the Excise Tax.

Definitions

Separation from Service. For purposes of this letter, "Separation from Service" means a "separation from service" within the meaning of Section 409A of the Code. Each installment payment provided under this letter shall at all times be considered a separate and distinct payment for purposes of Section 409A of the Code. Notwithstanding anything in this letter to the contrary, to the extent required to avoid a prohibited distribution under Section 409A of the Code, the benefits provided under this letter will not be provided to you until the earlier of (a) the expiration of the six-month period measured from the date of your Separation from Service with the Company or (b) the date of your death. Upon the first business day after expiration of the relevant period, all payments delayed pursuant to the preceding sentence will be paid in a lump sum and any remaining payments due will be paid as otherwise provided herein.

Cause. "Cause" shall mean the occurrence of any of the following events by the individual: (i) commission of any crime involving the Company, or any crime involving fraud, breach of trust, or physical or emotional harm to any person, moral turpitude or dishonesty; (ii) any unauthorized use or disclosure of the Company's proprietary information (other than any such use or disclosure that is not intentional and is not material); (iii) any intentional misconduct or gross negligence that has a material adverse effect on the Company's business or reputation; (iv) any material breach by you of any agreement between you and the Company that is not cured within thirty (30) days after receipt of written notice from the Company describing any such breach; or (v) repeated and willful failure to perform the duties, functions and responsibilities of the individual's position after a written warning from the Company.

Good Reason. "Good Reason" shall mean your resignation from all positions you then hold with the Company if: (A) without your written consent (i) there is a material diminution in the nature or scope of your responsibilities, duties, authority, or title; (ii) there is a material reduction of your base salary; provided, however, that a material reduction in your base salary pursuant to a salary reduction program affecting all or substantially all of the employees of the Company and that does not adversely affect you to a greater extent than other similarly situated employees shall not constitute Good Reason; or (iii) you are required to relocate your primary work location to a facility or location that would increase your one way commute distance by more than thirty-five (35) miles from your primary work location as of immediately prior to such change, (B) you provide written notice outlining such conditions, acts or omissions to

the Company's Chief Executive Officer, President, Chief Financial Officer or General Counsel within thirty (30) days immediately following such material change or reduction, (C) such material change or reduction is not remedied by the Company within thirty (30) days following the Company's receipt of such written notice and (D) your resignation is effective not later than thirty (30) days after the expiration of such thirty (30) day cure period. "Good Reason" shall also mean your resignation, at your sole discretion, on the one year anniversary of a Change of Control from all positions you then hold with the Company or its successor if by that date (i) you have not entered into a written

letter or agreement with the Company or such successor that provides for your continued employment with the Company or such successor, and (ii) if at that one year anniversary of a Change of Control, another Chief Financial Officer has any control and/or oversight, directly or indirectly, over the Company (or what used to be the Company prior to such transaction). For purposes of clarification, any Qualifying Termination that occurs on the first anniversary of a Change of Control shall be deemed and treated as occurring within the twelve (12) months immediately following a Change of Control for all purposes of this letter.

Invention, Non-Disclosure, Non-Competition and Non-Solicitation Obligations. You previously have executed and delivered the Company's standard form of Employee Proprietary Information, Inventions, Non-Competition and Non-Solicitation Agreement (the "NDA"), an executed copy of which is attached hereto as Exhibit A.

At-Will Employment. This letter shall not be construed as an agreement, either express or implied, to employ you for any stated term, and shall in no way alter the Company's policy of employment at-will. Similarly, nothing in this letter shall be construed as an agreement, either express or implied, to pay you any compensation or grant you any benefit beyond the end of your employment with the Company, except as otherwise explicitly set forth in this letter. This letter supersedes all prior understandings, whether written or oral, including, without limitation, your current employment agreement, with respect to the subject matter of this letter.

[The remainder of this page is intentionally left blank.]



Please indicate your acceptance of this letter agreement by signing below in the space provided for your signature.

Sincerely,

/s/ Keith M. Gottesdiener

Keith M. Gottesdiener
Chief Executive Officer

The foregoing correctly sets forth the terms of my at-will employment with the Company. I am not relying on any representations other than those set forth above.

/s/ Hunter Smith

September 13, 2017

Hunter Smith

Date



EXHIBIT A

EXECUTED NDA

[See attached]

EMPLOYEE PROPRIETARY INFORMATION, INVENTIONS, NON-COMPETITION AND NON-SOLICITATION AGREEMENT

In consideration and as a condition of my employment, or continued employment, by Rhythm Pharmaceuticals, Inc., a Delaware corporation (the “Company”), and the compensation now and hereafter paid to me, I hereby agree as follows:

1. nondisclosure

1.1 Recognition of Company’s Rights; Nondisclosure. At all times during my employment by the Company and thereafter, I will hold in strictest confidence and will not disclose, use, lecture upon, or publish any of the Company’s Proprietary Information (defined below), except as such disclosure, use, lecture, or publication may be required in connection with my work for the Company, or unless any other individual that is an officer of the Company expressly authorizes such in writing. I will obtain the Company’s prior written approval before publishing or submitting for publication any material (written, oral, or otherwise) that relates to my work at the Company or incorporates any Proprietary Information. Notwithstanding the foregoing, disclosure of any such Proprietary Information shall not be prohibited if such disclosure is directly related to a valid and existing order of a court or other governmental body or agency; *provided, however,* that I shall have first given prompt notice to the Company of any possible or prospective order and the Company shall have been afforded a reasonable opportunity to prevent or limit any such disclosure. I hereby assign to the Company any rights I may have or acquire in any Proprietary Information and recognize that all Proprietary Information shall be the sole property of the Company and its assigns.

1.2 Proprietary Information. The term “Proprietary Information” means any and all confidential or proprietary knowledge, data or information of the Company or any of its subsidiaries or controlled affiliates. By way of illustration but not limitation, “Proprietary Information” includes: (a) developments, inventions, ideas, data, programs, other works of authorship, designs and techniques, trade secrets, mask works, processes, formulas, source and object codes, algorithms, compositions of matter, chemical structures, formulations, methods (including, without limitation, methods of use, delivery or manufacture), dosing regimens, know-how, technology, improvements and discoveries (hereinafter collectively referred to as “Inventions”); (b) the design of, and all other information with respect to, preclinical studies and clinical trials, including, without limitation, the results of such preclinical studies and clinical trials; (c) clinical development and regulatory approval strategy; (d) information regarding research collaborations, joint development relationships, licensing relationships and transactions, corporate partnering relationships and transactions, joint ventures and other strategic alliances, including, without limitation, the research, development and commercialization activities, areas or fields subject to such relationships or transactions, the results of such research, development or commercialization activities and the terms of any agreements entered into by the Company or any of its subsidiaries or controlled affiliates in connection with such relationships or transactions; (e) information regarding plans for research, development, new services or products, marketing and selling, business plans, budgets and unpublished financial statements, licenses, prices and costs, clients, customers, and suppliers; and (f) information regarding the skills and compensation of the employees and/or consultants of the Company or any of its subsidiaries or controlled

affiliates. For purposes of this Employee Proprietary Information, Inventions, Non-Competition and Non-Solicitation Agreement (this “Agreement”), the term “Proprietary Information” shall not include information which is or becomes publicly available without breach of: (i) this Agreement; (ii) any other agreement or instrument to which the Company or any of its subsidiaries or controlled affiliates is a party or a beneficiary; or (iii) any duty owed to the Company or any of its subsidiaries or controlled affiliates by me or by any third party; *provided, however,* that if I shall seek to disclose, use, lecture upon, or publish any Proprietary Information, I shall bear the burden of proving that any such information shall have become publicly available without any such breach.

1.3 Third Party Information. I understand that the Company or any of its subsidiaries or controlled affiliates has received and in the future will receive from third parties confidential or proprietary information (“Third Party Information”) subject to a duty to maintain the confidentiality of such information and to use it only for certain limited purposes. During the term of my employment by the Company and thereafter, I will hold Third Party Information in the strictest confidence and will not disclose Third Party Information to anyone (other than personnel of the Company or any of its subsidiaries or controlled affiliates who need to know such information in connection with their work for the Company or any of its subsidiaries or controlled affiliates) and will not use Third Party Information (except in connection with my work for the Company or any of its subsidiaries or controlled affiliates), unless and to the extent that any other individual that is an officer of the Company expressly authorizes such disclosure or use in writing. I hereby assign to the Company any rights I may have or acquire in any Third Party Proprietary Information during my employment with the Company.

1.4 No Improper Use of Information of Prior Employers and Others. During my employment by the Company, I will not improperly use or disclose any confidential information or trade secrets, if any, of any former employer or any other person to whom I have an obligation of confidentiality, and I will not bring onto the premises of the Company or any of its subsidiaries or controlled affiliates any unpublished documents or any property belonging to any former employer or any other person to whom I have an obligation of confidentiality unless consented to in writing by that former employer or person. I will use in the performance of my duties only information which is generally known and used by persons with training and experience comparable to my own, which is common knowledge in the industry or otherwise legally in the public domain, or which is otherwise provided or developed by, or on behalf of, the Company or any of its subsidiaries or controlled affiliates.

1.5 Defend Trade Secrets Act. Pursuant to 18 U.S.C. § 1833(b), I will not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of a trade secret of the Company or its affiliates that (a) I make (i) in confidence to a Federal, State, or local government official, either directly or indirectly, or to my attorney and (ii) solely for the purpose of reporting or investigating a suspected violation of law; or (b) I make in a complaint or other document that is filed under seal in a lawsuit or other proceeding. If I file a lawsuit for retaliation by the Company for reporting a suspected violation of law, I may disclose the trade secret to my attorney and use the trade secret information in the court proceeding, if I (x) file any document containing the trade secret under seal, and (y) do not disclose the trade secret, except pursuant to court order. Nothing in this Agreement is intended to conflict with 18 U.S.C. § 1833(b) or create liability for disclosures of trade secrets that are expressly allowed by 18 U.S.C. § 1833(b).

2. Assignment of Inventions

2.1 Proprietary Rights. The term “Proprietary Rights” means all trade secret, patent, copyright, mask work and other intellectual property rights throughout the world.

2.2 Prior Inventions. Inventions, if any, patented or unpatented, which I made prior to the commencement of my employment with the Company are excluded from the scope of this Agreement. To preclude any possible uncertainty, I have set forth on Exhibit A (Prior Inventions) attached hereto a complete list of all Inventions that I have, alone or jointly with others, conceived, developed or reduced to practice or caused to be conceived, developed or reduced to practice prior to the commencement of my employment with the Company, that I consider to be my property or the property of third parties and that I wish to have excluded from the scope of this Agreement (collectively referred to as "Prior Inventions"). If disclosure of any such Prior Invention would cause me to violate any prior confidentiality agreement, I understand that I am not to list such Prior Inventions in Exhibit A but am only to disclose a cursory name for each such invention, a listing of the party or parties to whom it belongs, and the fact that full disclosure as to such inventions has not been made for that reason. A space is provided on Exhibit A for such purpose. If I do not attach such disclosure, I am representing thereby that there are no Prior Inventions. If, in the course of my employment with the Company, I incorporate a Prior Invention (whether or not such Prior Invention is listed in Exhibit A) into a product, compound, composition of matter, chemical structure, biological material, formulation, method, process or machine of the Company or any of its subsidiaries or controlled affiliates, or I in any way otherwise use, or make available for use, a Prior Invention (whether or not such Prior Invention is listed in Exhibit A) in connection with the research, development, manufacture, use or commercialization of any such product, compound, composition of matter, chemical structure, biological material, formulation, method, process or machine, the Company is hereby granted and shall have a nonexclusive, royalty free, irrevocable, perpetual, worldwide license (with rights to sublicense through multiple tiers of sublicensees) to research, cause to be researched, develop, cause to be developed, make, cause to be made, modify, cause to be modified, use, cause to be used and sell or otherwise commercialize, or cause to be sold or otherwise commercialized, such Prior Invention. Notwithstanding the foregoing, I agree that I will not incorporate, or permit to be incorporated, Prior Inventions in any Company Inventions (as defined in Section 2.3 below), or in any product, compound, composition of matter, chemical structure, biological material, formulation, method, process or machine of the Company or any of its subsidiaries or controlled affiliates, without the Company's prior written consent.

2.3 Assignment of Inventions. Subject to this Section 2.3 and to Sections 2.5 and 2.6, I hereby assign to the Company all my right, title and interest in and to any and all Inventions (and all Proprietary Rights with respect thereto), whether or not patentable or registrable under copyright or similar statutes, that are made, conceived, reduced to practice or learned by me, either alone or jointly with others, (i) in the course of my employment with the Company, (ii) during the term of my employment with the Company (whether or not in the course of my employment with the Company and whether or not during regular business hours) if and to the extent that any such Invention relates to the actual business or planned business of the Company or was made, conceived or reduced to practice by me, either alone or jointly with others, as a result of any material use of any of the properties, assets or facilities of the Company or (iii) arising out of, based upon, or resulting from the use of, any Proprietary Information or Third-Party Proprietary Information made available to me or to which I had access as an employee of the Company. Inventions assigned pursuant to this Section 2 to the Company, or to a third party as directed by

the Company pursuant to Section 2.5 below, are hereinafter referred to as "Company Inventions." At the request of the Company at any time and from time to time, I will execute and deliver any and all instruments, documents and agreements reasonably requested by the Company for purposes of confirming my assignment to the Company of all of my right, title and interest in and to any and all Company Inventions (and all Proprietary Rights with respect thereto), including, without limitation, at any time when any such Company Inventions (or any Proprietary Rights with respect thereto) are first reduced to practice or first fixed in a tangible medium, as applicable.

For the avoidance of doubt, notwithstanding any contrary provision contained herein, nothing contained in this Agreement shall require the assignment of any Invention (or Proprietary Right with respect thereto) made or conceived by me during the period of my employment to the extent such assignment is prohibited by any applicable state or federal law.

2.4 Obligation to Keep Company Informed. During the period of my employment with the Company and thereafter, I will promptly disclose to the Company fully and in writing all Company Inventions authored, conceived or reduced to practice by me, either alone or jointly with others. In addition, during the period of my employment with the Company and thereafter, I will promptly disclose to the Company all patent applications filed by me or on my behalf that claim any Company Invention.

2.5 Government or Third Party. I also agree to assign all my right, title and interest in and to any particular Company Invention to a third party, including without limitation the United States, as directed by the Company.

2.6 Works for Hire. I acknowledge that all original works of authorship which are made by me (solely or jointly with others) within the scope of my employment with the Company and which are protectable by copyright are "works made for hire," pursuant to the United States Copyright Act (17 U.S.C., Section 101).

2.7 Enforcement of Proprietary Rights. I will assist the Company in every proper way in obtaining, and from time to time enforcing, United States and foreign Proprietary Rights relating to Company Inventions in any and all countries. To that end I will promptly execute, verify and deliver such documents and perform such other acts (including appearances as a witness) as the Company may reasonably request for use in applying for, obtaining, perfecting, evidencing, sustaining and enforcing such Proprietary Rights and the assignment thereof. In addition, I will promptly execute, verify and deliver assignments of such Proprietary Rights to the Company or its designee. My obligation to assist the Company with respect to Proprietary Rights relating to such Company Inventions in any and all countries shall continue beyond the termination of my employment with the Company, but the Company shall compensate me at a reasonable rate after my termination for the time actually spent by me at the Company's request on such assistance.

In the event the Company is unable for any reason, after reasonable effort, to secure my signature on any document needed in connection with the actions specified in the preceding paragraph, I hereby irrevocably designate and appoint the Company and its duly authorized officers and agents as my agents and attorneys-in-fact, subject to full power or substitution and resubstitution, which appointment is coupled with an interest, to act for and in my behalf to execute, verify and file any such documents and to do all other lawfully permitted acts to further the purposes of the preceding paragraph with the same legal force and effect as if executed by me. I hereby waive and quitclaim

to the Company any and all claims, of any nature whatsoever, which I now or may hereafter have for infringement of any Proprietary Rights assigned hereunder to the Company.

3. RECORDS. I agree to keep and maintain adequate and current records (in the form of notes, memoranda, sketches, drawings and in any other form that may be required by the Company) of all Proprietary Information and all Company Inventions made, conceived, developed or reduced to practice by me, which records shall be available to and remain the sole property of the Company at all times.

4. NON-SOLICITATION. I agree that, during the period of my employment with the Company and for the one (1) year period after the date my employment with the Company ends for any reason, including but not limited to voluntary termination by me or termination by the Company, I will not, for myself or for the benefit of any other person (including, without limitation, any other person with which I may have a direct or indirect interest or relationship as an employee, consultant, advisor, equityholder or otherwise): (a) solicit, hire or engage, or attempt to solicit, hire or engage, any individual as an employee, consultant, advisor, officer, manager, managing partner, director or in any other similar capacity if such individual shall have been an employee of the Company or any of its subsidiaries or controlled affiliates at any time during the one (1) year period prior to the date of termination of my employment with the Company; (b) solicit, induce or attempt to induce any customer, vendor, contractor, consultant or advisor of the Company or any of its subsidiaries or controlled affiliates to terminate, diminish, or materially alter his, her or its relationship with the Company or any of its subsidiaries or controlled affiliates; or (c) solicit, induce or attempt to induce any potential customer, vendor, contractor, employee, consultant or advisor whose identity and potential relationship with the Company or any of its subsidiaries or controlled affiliates I learned as a result of my employment with the Company, not to establish, or to diminish or materially alter, such potential relationship with the Company or any of its subsidiaries or controlled affiliates. In the event that a court finds this Section 4, or any of its restrictions, to be unenforceable or invalid, I and the Company agree that (i) this Section 4 will be automatically modified to provide the Company with the maximum protection of its business interests allowed by law and (ii) I shall be bound, and such court shall enforce, this Section 4 as so modified.

5. NON-COMPETITION. I agree that, during the term of my employment with the Company and for the one (1) year period after the date my employment with the Company ends for any reason, including but not limited to voluntary termination by me or termination by the Company, I will not, directly or indirectly, as an officer, director, manager, employee, consultant, advisor, owner, partner, member, stockholder, or in any other capacity, (a) compete with the business or planned business of the Company or any of its subsidiaries or controlled affiliates, or (b) take any steps or actions to facilitate or prepare for competition with the business or planned business of the Company or any of its subsidiaries or controlled affiliates, nor will I assist another person to take any action that I would be prohibited from taking under this Section 5. The obligations not to compete that I have undertaken under this Section 5 shall apply in all countries of the world. For purposes of this Section 5, I will not be deemed or treated as being in competition with the business or planned business of the Company or any of its subsidiaries or controlled affiliates or as being in violation of the covenant set forth in the clause (b) above in this Section 5 merely by virtue of my ownership of any equity interest in any business or person that is in competition with, or is planning to be in competition with, the business or planned business of the Company or any of its subsidiaries or controlled affiliates, if my ownership of any such equity interest represents

five percent (5%) or less the total equity interests in such business or person. I hereby acknowledge and agree that the foregoing restrictions contained in this Section 5 are reasonable, proper and necessitated by the legitimate business interests of the Company and will not prevent me from earning a living or pursuing my career. In the event that a court finds this Section 5, or any of its restrictions, to be unenforceable or invalid, I and the Company agree that (i) this Section 5 will be automatically modified to provide the Company with the maximum protection of its business interests allowed by law and (ii) I shall be bound, and such court shall enforce, this Section 5 as so modified. The parties agree that for the purposes of this Agreement, "business", and/or "planned business" shall mean development of MC4R agonists for the treatment of human disease.

6. NO CONFLICTING OBLIGATION. I represent that my performance of all the terms of this Agreement and as an employee of the Company has not breached, and does not and will not breach, any agreement to keep in confidence information acquired by me in confidence or in trust prior to, or outside the scope of, my employment by the Company and any agreement not to compete with the business of any third party. I have not entered into, and I agree I will not enter into, any agreement, either written or oral, in conflict herewith.

7. RETURN OF COMPANY DOCUMENTS. When I leave the employ of the Company, I will deliver to the Company any and all notes, memoranda, specifications, drawings, devices, formulas, and documents, together with all copies thereof, and any other material containing or disclosing any Company Inventions, Third Party Information or Proprietary Information of the Company. I further agree that, during the term of my employment with the Company or at any time thereafter, any property situated on the premises of the Company or any of its subsidiaries or controlled affiliates, including disks and other storage media, filing cabinets or other work areas, is subject to inspection by Company personnel at any time with or without notice. In the event I leave the employ of the Company for any reason whatsoever, I will promptly sign and deliver the "Termination Certificate" attached hereto as Exhibit B.

8. LEGAL AND EQUITABLE REMEDIES. Because my services are personal and unique and because I may have access to and become acquainted with the Proprietary Information of the Company, the Company shall have the right to enforce this Agreement and any of its provisions by injunction, specific performance, or other equitable relief, without bond and without prejudice to any other rights and remedies that the Company may have for a breach of this Agreement. In the event that the Company enforces the provisions of Section 4 or Section 5 hereof through a court order, I agree that the restrictions contained in Section 4 or Section 5, as the case may be, shall remain in effect for a period of one year from the effective date of such court order. I agree that if the Company is successful in whole or in part in any legal or equitable action against me under this Agreement, the Company shall be entitled to recover from me all costs, including reasonable attorney's fees, incurred by the Company in connection with such legal or equitable action.

9. NOTICES. Any notices required or permitted hereunder shall be given to the appropriate party at the address specified below or at such other address as the party shall specify in writing. Such notice shall be deemed given upon personal delivery to the appropriate address, one (1) business day after dispatch if sent by nationally recognized courier or overnight delivery service, on the date of dispatch if sent by facsimile or electronic mail for which confirmation of transmission is provided or, if sent by certified or registered mail, three (3) business days after the date of mailing.

10. NOTIFICATION OF NEW EMPLOYER. In the event that I leave the employ of the Company and accept new employment, I hereby agree to notify my new employer of my rights and obligations under this Agreement and I hereby consent to the Company or any person on behalf of the Company providing notice to my new employer of such rights and obligations.

11. GENERAL PROVISIONS

11.1 Governing Law; Consent to Personal Jurisdiction. This Agreement will be governed by and construed according to the laws of the Commonwealth of Massachusetts, as such laws are applied to agreements entered into and to be performed entirely within Massachusetts between Massachusetts residents. I hereby expressly consent to the personal jurisdiction of the state and federal courts located in the Commonwealth of Massachusetts for any lawsuit filed there against me by the Company arising from or related to this Agreement.

11.2 Severability. In case any one or more of the provisions contained in this Agreement shall, for any reason, be held to be invalid, illegal, or unenforceable in any respect, such invalidity, illegality, or unenforceability shall not affect the other provisions of this Agreement, and this Agreement shall be construed as if such invalid, illegal, or unenforceable provision had never been contained herein. Moreover, if any one or more of the provisions contained in this Agreement shall for any reason be held to be excessively broad as to duration, geographical scope, activity or subject, it shall be construed by limiting and reducing it, so as to be enforceable to the extent compatible with the applicable law as it shall then appear.

11.3 Successors and Assigns. This Agreement will be binding upon my heirs, executors, administrators and other legal representatives and will be for the benefit of the Company, its successors, and its assigns. Without limiting the generality of the foregoing, if I become an employee of any subsidiary or controlled affiliate of the Company, then (i) such subsidiary or controlled affiliate shall be deemed and treated as an intended third party beneficiary of this Agreement to the same extent as if such subsidiary or controlled affiliate were a party to this Agreement and (ii) each reference in this Agreement to the term "Company" shall be deemed to be a reference to whichever of Rhythm Pharmaceuticals, Inc. and/or such subsidiary, parent or controlled affiliate is my employer.

11.4 Survival. The provisions of this Agreement shall survive the termination of my employment with the Company and the assignment of this Agreement by the Company to any successor in interest or other assignee.

11.5 Employment. I agree and understand that nothing in this Agreement shall confer any right with respect to continuation of my employment by the Company, nor shall it interfere in any way with my right or the Company's right to terminate my employment at any time, with or without cause.

11.6 Waiver. No waiver by the Company of any breach of this Agreement shall be a waiver of any preceding or succeeding breach. No waiver by the Company of any right under this Agreement shall be construed as a waiver of any other right. The Company shall not be required to give notice to enforce strict adherence to all terms of this Agreement.

11.7 Entire Agreement. My obligations, and the Company's rights, under this Agreement shall apply to any time during which I was previously employed, or am in the future

employed, by the Company. This Agreement is the final, complete and exclusive agreement of the parties with respect to the subject matter hereof and supersedes all prior agreements relating to the subject matter hereof and merges all prior discussions between us. No modification of or amendment to this Agreement, nor any waiver of any rights under this Agreement, will be effective unless in writing and signed by the party to be charged. Any subsequent change or changes in my duties, salary or compensation will not affect the validity or scope of this Agreement.

11.8 Counterparts. This Agreement may be signed in counterparts, each shall be deemed an original and shall together constitute one agreement.

11.9 Acknowledgement. I acknowledge that this Agreement is a condition to my employment with the Company and that I have had a full and adequate opportunity to read, understand and discuss with my advisors, including legal counsel, the terms and conditions contained in this Agreement prior to signing hereunder.

This Agreement shall be effective as of the first day of my employment with the Company.

[Remainder of page intentionally left blank]

I HAVE READ THIS AGREEMENT CAREFULLY AND UNDERSTAND ITS TERMS. I HAVE COMPLETELY FILLED OUT EXHIBITA TO THIS AGREEMENT.

Dated: July 18, 2017

/s/ Hunter Smith

Name: Hunter Smith

Address: 17 Myanos Road
New Canaan, CT 06840

ACCEPTED AND AGREED:

RHYTHM PHARMACEUTICALS, INC.

By: /s/ Keith Gottesdiener

Name: Keith Gottesdiener
Title: Chief Executive Officer

Dated:

EXHIBIT A

TO: Rhythm Pharmaceuticals, Inc.

FROM:

DATE:

SUBJECT: Prior Inventions

1. Except as listed in Section 2 below, the following is a complete list of all inventions or improvements relevant to the subject matter of my employment by Rhythm Pharmaceuticals, Inc. (the “Company”) that have been made or conceived or first reduced to practice by me alone or jointly with others prior to my employment by the Company:
 - o No inventions or improvements.
 - o See below:
 - o Additional sheets attached.
2. Due to a prior confidentiality agreement, I cannot complete the disclosure under Section 1 above with respect to inventions or improvements generally listed below, the proprietary rights and duty of confidentiality with respect to which I owe to the following party(ies):

Invention or Improvement	Party(ies)	Relationship
1.		
2.		
3.		

- o Additional sheets attached.
3. I acknowledge that this Exhibit A, if completed, forms a part of the Employee Proprietary Information, Inventions, Non-Competition and Non-Solicitation Agreement to which the Company and I are parties and that the failure to complete this Exhibit A and cause it to be attached to such Agreement constitutes a representation by me that I have no Prior Inventions.

EXHIBIT B

TERMINATION CERTIFICATE

I hereby confirm and certify to the Company that I have returned to the Company all Proprietary Information in my possession or control, that I have disclosed fully to the Company all Company Inventions and that I have and will comply fully with all of my obligations to the Company under my Employee Proprietary Information, Inventions, Non-Competition and Non-Solicitation Agreement with the Company.

Name:



Rhythm Pharmaceuticals, Inc.
500 Boylston Street – 11th Floor
Boston, MA 02116
Main Telephone: 617-585-2090
www.rhythmtx.com

September 13, 2017

Nithya Desikan
c/o Rhythm Pharmaceuticals, Inc.
500 Boylston Street, 11th Floor
Boston, MA 02116

Dear Nithya:

On behalf of Rhythm Pharmaceuticals, Inc., formerly known as Rhythm Metabolic, Inc. (the “Company” or “Rhythm”), I am pleased to set forth below the amended and restated terms of your employment with the Company.

Employment. You are currently the Chief Commercial Officer of the Company, and during the term of your employment with the Company, you will continue to hold the position and title of Chief Commercial Officer. During the term of your employment with the Company, you will be responsible for performing the duties associated with the position above or as the Company may otherwise assign to you. Your primary place of employment initially will be in the Company’s offices located in Boston, Massachusetts; however, you will be expected to travel as may be necessary to fulfill your responsibilities. In the course of your employment with the Company, you will be subject to, and required to comply with, all Company policies and all applicable laws and regulations.

Base Salary. During your employment, your salary will be \$360,000 annualized, subject to all required and elected taxes and other withholdings. Your salary may be adjusted from time to time in accordance with normal business practice and in the sole discretion of the Company.

Annual Incentive Bonus. Following the end of each fiscal year and subject to the approval by the Company’s Board of Directors, you will be eligible to earn an incentive bonus, based on your performance and the Company’s performance, each during the applicable fiscal year, if your employment continues in good standing on the date of payment of such incentive bonus. Your target annual incentive bonus opportunity shall be 30% of your annualized base salary, provided that, from and after the closing of the Company’s first underwritten public offering of its Common Stock under the Securities Act, if any (the “IPO”), your target annual incentive bonus opportunity shall be 35% of your annualized base salary.

Equity Grant. Any existing grants of equity you have in the Company will be treated consistent with the terms of the applicable agreements under which such awards have been granted. You may be awarded additional equity grants from time to time in accordance with normal business practice and in the sole discretion of the Company’s Board of Directors. The terms of any future equity grant will be consistent with any plan under which they are granted and the terms of the applicable agreement for the award(s).

Benefits. You may participate in any and all benefit programs that the Company establishes and makes available to its employees from time to time, subject to the terms and conditions of those programs. The Company’s benefits programs are subject to change at any time in the Company’s sole discretion.

Vacation. You will be entitled to annual paid vacation of four (4) weeks. Your accrual and use of vacation time will be pursuant to any vacation or time off policy the Company may establish or modify from time to time. The Company’s vacation policy is subject to change at any time in the Company’s sole discretion.

Severance. If the Company terminates your employment without Cause (as defined below) or you resign your employment with the Company for Good Reason (as defined below) (in either event, a “Qualifying Termination”), then, subject to your execution of a reasonable release acceptable to the Company (the “Release”), the expiration of any revocation period provided in the Release and your continued compliance with the terms of the NDA (as defined below), the Company will pay you an amount (the “Regular Severance Amount”) equal to your then-current base salary rate for a period of six (6) months, provided that, (i) if any such Qualifying Termination occurs at any time after the IPO, if any, the Regular Severance Amount shall be an amount equal to your then-current base salary rate for a period of nine (9) months, and (ii) if any such Qualifying Termination occurs an, or at any time prior to, the first anniversary of the start date of your employment with the Company (even if such first anniversary occurs after the IPO), the Regular Severance Amount shall be an amount equal to your then-current base salary rate for a period of twelve (12) months.

If there is a Qualifying Termination within the three (3) months immediately preceding or the twelve (12) months immediately following a Change of Control (as defined in the Company’s 2015 Equity Incentive Plan, as may be amended and in effect from time to time or succeeded or superseded by a successor equity incentive plan), then, subject to your execution of a Release following your Separation from Service (as defined below), the expiration of any revocation period provided in the Release and your continued compliance with the terms of the NDA, the Company will pay you, in lieu of any Regular Severance Amount, an amount (the “Change of Control Severance Amount”) equal to your then-current base salary rate for a period of twelve (12) months plus an amount equal to 100% of your then-applicable target annual incentive bonus.

Any severance amount to which you may be entitled under this letter will be paid in substantially equal installments in accordance with the Company's ordinary payroll practices, beginning on the first payroll date following the date that is either (i) sixty (60) days after the date of your Separation from Service or (ii) in the case of a Separation from Service that is a Qualifying Termination that occurs within three (3) months immediately preceding a Change of Control, sixty (60) days after such Change of Control, provided that, in the case of either of the foregoing clauses (i) and (ii), the Company, in its sole discretion, may have the option to pay any such severance amount to you as a lump sum. To be eligible for either the Regular Severance Amount or the Change of Control Severance Amount, as applicable, you must execute and deliver the Release to the Company and allow it to become effective within thirty (30) days of your Separation from Service or, if later, within thirty (30) days of a Change of Control giving rise to a Change of Control Severance Amount entitlement.

In addition, if following your Separation from Service, you are eligible for and timely elect continued medical insurance coverage pursuant to COBRA, the Company will reimburse you for the applicable premiums for you and your eligible dependents during the period commencing on the date of your Separation from Service and ending on the earlier to occur of (a) the final day of the applicable severance period and (b) the date you otherwise become ineligible for continued coverage under COBRA. Notwithstanding the foregoing, if the Company determines that it cannot provide such reimbursement of premiums to you without potentially violating applicable law, the Company shall not be obligated to make any such payments or reimbursements to you.

If the Qualifying Termination occurs within the three (3) months immediately preceding or the twelve (12) months immediately following a Change of Control, then each outstanding equity award in the Company held by you shall immediately vest and, if applicable, become exercisable with respect to one hundred percent (100%) of the shares of equity of the Company subject thereto. The foregoing provisions of this paragraph shall apply notwithstanding anything express or implied to the contrary in any agreement or award between you and the Company, or in any plan of the Company, that is applicable to such outstanding equity award.

Notwithstanding anything herein to the contrary, in the event that any compensation or benefit that constitutes "nonqualified deferred compensation" within the meaning of Section 409A of the Internal Revenue Code of 1986, as amended (the "Code"), becomes payable upon the occurrence of a Change of Control, such compensation or benefit shall not be paid unless such Change of Control constitutes a "change in control event" within the meaning of Section 409A of the Code.

If any payment or benefit you would receive under this letter, when combined with any other payment or benefit you receive pursuant to the termination of your employment with the Company ("Payment") would (i) constitute a "parachute payment" within the meaning of Section 280G of the Code, and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax"), then such Payment shall be either (x) the full amount of such Payment or (y) such lesser amount (with your choice of whether to reduce cash payments or stock option compensation or both) as would result in no portion of the Payment being subject to the Excise Tax, whichever of the foregoing amounts, taking into account the applicable federal, state and local employment taxes, income taxes and the Excise Tax results in your receipt, on an after-tax basis, of the greater amount of the Payment notwithstanding that all or some portion of the Payment may be subject to the Excise Tax.

Definitions

Separation from Service. For purposes of this letter, "Separation from Service" means a "separation from service" within the meaning of Section 409A of the Code. Each installment payment provided under this letter shall at all times be considered a separate and distinct payment for purposes of Section 409A of the Code. Notwithstanding anything in this letter to the contrary, to the extent required to avoid a prohibited distribution under Section 409A of the Code, the benefits provided under this letter will not be provided to you until the earlier of (a) the expiration of the six-month period measured from the date of your Separation from Service with the Company or (b) the date of your death. Upon the first business day after expiration of the relevant period, all payments delayed pursuant to the preceding sentence will be paid in a lump sum and any remaining payments due will be paid as otherwise provided herein.

Cause. "Cause" shall mean the occurrence of any of the following events by the individual: (i) commission of any crime involving the Company, or any crime involving fraud, breach of trust, or physical or emotional harm to any person, moral turpitude or dishonesty; (ii) any unauthorized use or disclosure of the Company's proprietary information (other than any such use or disclosure that is not intentional and is not material); (iii) any intentional misconduct or gross negligence that has a material adverse effect on the Company's business or reputation; (iv) any material breach by you of any agreement between you and the Company that is not cured within thirty (30) days after receipt of written notice from the Company describing any such breach; or (v) repeated and willful failure to perform the duties, functions and responsibilities of the individual's position after a written warning from the Company.

Good Reason. "Good Reason" shall mean your resignation from all positions you then hold with the Company if: (A) without your written consent (i) there is a material diminution in the nature or scope of your responsibilities, duties, authority, or title; (ii) there is a material reduction of your base salary; provided, however, that a material reduction in your base salary pursuant to a salary reduction program affecting all or substantially all of the employees of the Company and that does not adversely affect you to a greater extent than other similarly situated employees shall not constitute Good Reason; or (iii) you are required to relocate your primary work location to a facility or location that would increase your one way commute distance by more than thirty-five (35) miles from your primary work location as of immediately prior to such change, (B) you provide written notice outlining such conditions, acts or omissions to the Company's Chief Executive Officer, President, Chief Financial Officer or General Counsel within thirty (30) days immediately following such material change or reduction, (C) such material change or reduction is not remedied by the Company within thirty (30) days following the Company's receipt of such written notice and (D) your resignation is effective not later than thirty (30) days after the expiration of such thirty (30) day cure period. "Good Reason" shall also mean your resignation on the one year anniversary of a Change of Control from all positions you then hold with the Company or its successor if by that date you have not entered into a written letter or agreement with the Company or such successor that provides for your continued employment with the Company or such successor. For purposes of clarification, any Qualifying Termination that occurs on the first anniversary of a Change of Control shall be deemed and treated as occurring within the twelve (12) months immediately following a Change of Control for all purposes of this letter.

Invention, Non-Disclosure, Non-Competition and Non-Solicitation Obligations. You previously have executed and delivered the Company's standard form of Employee Proprietary Information, Inventions, Non-Competition and Non-Solicitation Agreement (the "NDA"), an executed copy of which is attached hereto as Exhibit A.

At-Will Employment. This letter shall not be construed as an agreement, either express or implied, to employ you for any stated term, and shall in no way alter the Company's policy of employment at-will. Similarly, nothing in this letter shall be construed as an agreement, either express or implied, to pay you any compensation or grant you any benefit beyond the end of your employment with the Company, except as otherwise explicitly set forth in this letter. This letter supersedes all prior understandings, whether written or oral, including, without limitation, your current employment agreement, with respect to the subject matter of this letter.

[The remainder of this page is intentionally left blank.]



Please indicate your acceptance of this letter agreement by signing below in the space provided for your signature.

Sincerely,

/s/ Keith M. Gottesdiener

Keith M. Gottesdiener
Chief Executive Officer

The foregoing correctly sets forth the terms of my at-will employment with the Company. I am not relying on any representations other than those set forth above.

/s/ Nithya Desikan

September 13, 2017

Nithya Desikan

Date



EXHIBIT A

EXECUTED NDA

[See attached]

RHYTHM PHARMACEUTICALS, INC.

**EMPLOYEE PROPRIETARY INFORMATION, INVENTIONS, NON-COMPETITION
AND NON-SOLICITATION AGREEMENT**

In consideration and as a condition of my employment, or continued employment, by Rhythm Pharmaceuticals, Inc., a Delaware corporation (the “Company”), and the compensation now and hereafter paid to me, I hereby agree as follows:

1. NONDISCLOSURE

1.1 Recognition of Company’s Rights; Nondisclosure. At all times during my employment by the Company and thereafter, I will hold in strictest confidence and will not disclose, use, lecture upon, or publish any of the Company’s Proprietary Information (defined below), except as such disclosure, use, lecture, or publication may be required in connection with my work for the Company, or unless any other individual that is an officer of the Company expressly authorizes such in writing. I will obtain the Company’s prior written approval before publishing or submitting for publication any material (written, oral, or otherwise) that relates to my work at the Company or incorporates any Proprietary Information. Notwithstanding the foregoing, disclosure of any such Proprietary Information shall not be prohibited if such disclosure is directly related to a valid and existing order of a court or other governmental body or agency; *provided, however,* that I shall have first given prompt notice to the Company of any possible or prospective order and the Company shall have been afforded a reasonable opportunity to prevent or limit any such disclosure. I hereby assign to the Company any rights I may have or acquire in any Proprietary Information and recognize that all Proprietary Information shall be the sole property of the Company and its assigns.

1.2 Proprietary Information. The term “Proprietary Information” means any and all confidential or proprietary knowledge, data or information of the Company or any of its subsidiaries or controlled affiliates. By way of illustration but not limitation, “Proprietary Information” includes: (a) developments, inventions, ideas, data, programs, other works of authorship, designs and techniques, trade secrets, mask works, processes, formulas, source and object codes, algorithms, compositions of matter, chemical structures, formulations, methods (including, without limitation, methods of use, delivery or manufacture), dosing regimens, know-how, technology, improvements and discoveries (hereinafter collectively referred to as “Inventions”); (b) the design of,

and all other information with respect to, preclinical studies and clinical trials, including, without limitation, the results of such preclinical studies and clinical trials; (c) clinical development and regulatory approval strategy; (d) information regarding research collaborations, joint development relationships, licensing relationships and transactions, corporate partnering relationships and transactions, joint ventures and other strategic alliances, including, without limitation, the research, development and commercialization activities, areas or fields subject to such relationships or transactions, the results of such research, development or commercialization activities and the terms of any agreements entered into by the Company or any of its subsidiaries or controlled affiliates in connection with such relationships or transactions; (e) information regarding plans for research, development, new services or products, marketing and selling, business plans, budgets and unpublished financial statements, licenses, prices and costs, clients, customers, and suppliers; and (f) information regarding the skills and compensation of the employees and/or consultants of the Company or any of its subsidiaries or controlled

affiliates. For purposes of this Employee Proprietary Information, Inventions, Non-Competition and Non-Solicitation Agreement (this “Agreement”), the term “Proprietary Information” shall not include information which is or becomes publicly available without breach of: (i) this Agreement; (ii) any other agreement or instrument to which the Company or any of its subsidiaries or controlled affiliates is a party or a beneficiary; or (iii) any duty owed to the Company or any of its subsidiaries or controlled affiliates by me or by any third party; *provided, however,* that if I shall seek to disclose, use, lecture upon, or publish any Proprietary Information, I shall bear the burden of proving that any such information shall have become publicly available without any such breach.

1.3 Third Party Information. I understand that the Company or any of its subsidiaries or controlled affiliates has received and in the future will receive from third parties confidential or proprietary information (“Third Party Information”) subject to a duty to maintain the confidentiality of such information and to use it only for certain limited purposes. During the term of my employment by the Company and thereafter, I will hold Third Party Information in the strictest confidence and will not disclose Third Party Information to anyone (other than personnel of the Company or any of its subsidiaries or controlled affiliates who need to know such information in connection with their work for the Company or any of its subsidiaries or controlled affiliates) and will not use Third Party Information (except in connection with my work for the Company or any of its subsidiaries or controlled affiliates), unless and to the extent that any other individual that is an officer of the Company expressly authorizes such disclosure or use in writing. I hereby assign to the Company any rights I may have or acquire in any Third Party Proprietary Information during my employment with the Company.

1.4 No Improper Use of Information of Prior Employers and Others. During my employment by the Company, I will not improperly use or disclose any confidential information or trade secrets, if any, of any former employer or any other person to whom I have an obligation of confidentiality, and I will not bring onto the premises of the Company or any of its subsidiaries or controlled affiliates any unpublished documents or any property belonging to any former employer or any other person to whom I have an obligation of confidentiality unless consented to in writing by that former employer or person. I will use in the performance of my duties only information which is generally known and used by persons with training and experience comparable to my own, which is common knowledge in the industry or otherwise legally in the public domain, or which is otherwise provided or developed by, or on behalf of, the Company or any of its subsidiaries or controlled affiliates.

1.5 Defend Trade Secrets Act. Pursuant to 18 U.S.C. § 1833(b), I will not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of a trade secret of the Company or its affiliates that (a) I make (i) in confidence to a Federal, State, or local government official, either directly or indirectly, or to my attorney and (ii) solely for the purpose of reporting or investigating a suspected violation of law; or (b) I make in a complaint or other document that is filed under seal in a lawsuit or other proceeding. If I file a lawsuit for retaliation by the Company for reporting a suspected violation of law, I may disclose the trade secret to my attorney and use the trade secret information in the court proceeding, if I (x) file any document containing the trade secret under seal, and (y) do not disclose the trade secret, except pursuant to court order. Nothing in this Agreement is intended to conflict with 18 U.S.C. § 1833(b) or create liability for disclosures of trade secrets that are expressly allowed by 18 U.S.C. § 1833(b).

2. ASSIGNMENT OF INVENTIONS

2.1 Proprietary Rights. The term “Proprietary Rights” means all trade secret, patent, copyright, mask work and other intellectual property rights throughout the world.

2.2 Prior Inventions. Inventions, if any, patented or unpatented, which I made prior to the commencement of my employment with the Company are excluded from the scope of this Agreement. To preclude any possible uncertainty, I have set forth on Exhibit A (Prior Inventions) attached hereto a complete list of all Inventions that I have, alone or jointly with others, conceived, developed or reduced to practice or caused to be conceived, developed or reduced to practice prior to the commencement of my employment with the Company, that I consider to be my property or the property of third parties and that I wish to have excluded from the scope of this Agreement (collectively referred to as “Prior Inventions”). If disclosure of any such Prior Invention would cause me to violate any prior confidentiality agreement, I understand that I am not to list such Prior Inventions in Exhibit A but am only to disclose a cursory name for each such invention, a listing of the party or parties to whom it belongs, and the fact that full disclosure as to such inventions has not been made for that reason. A space is provided on Exhibit A for such purpose. If I do not attach such disclosure, I am representing thereby that there are no Prior Inventions. If, in the course of my employment with the Company, I incorporate a Prior Invention (whether or not such Prior Invention is listed in Exhibit A) into a product, compound, composition of matter, chemical structure, biological material, formulation, method, process or machine of the Company or any of its subsidiaries or controlled affiliates, or I in any way otherwise use, or make available for use, a Prior Invention (whether or not such Prior Invention is listed in Exhibit A) in connection with the research, development, manufacture, use or commercialization of any such product, compound, composition of matter, chemical structure, biological material, formulation, method, process or machine, the Company is hereby granted and shall have a nonexclusive, royalty free, irrevocable, perpetual, worldwide license (with rights to sublicense through multiple tiers of sublicensees) to research, cause to be researched, develop, cause to be developed, make, cause to be made, modify, cause to be modified, use, cause to be used and sell or otherwise commercialize, or cause to be sold or otherwise commercialized, such Prior Invention. Notwithstanding the foregoing, I agree that I will not incorporate, or permit to be incorporated, Prior Inventions in any Company Inventions (as defined in Section 2.3 below), or in any product, compound, composition of matter, chemical structure, biological material, formulation, method, process or machine of the Company or any of its subsidiaries or controlled affiliates, without the Company’s prior written consent.

2.3 Assignment of Inventions. Subject to this Section 2.3 and to Sections 2.5 and 2.6, I hereby assign to the Company all my right, title and interest in and to any and all Inventions (and all Proprietary Rights with respect thereto), whether or not patentable or registrable under copyright or similar statutes, that are made, conceived, reduced to practice or learned by me, either alone or jointly with others, (i) in the course of my employment with the Company, (ii) during the term of my employment with the Company (whether or not in the course of my employment with the Company and whether or not

during regular business hours) if and to the extent that any such Invention relates to the actual business or planned business of the Company or was made, conceived or reduced to practice by me, either alone or jointly with others, as a result of any material use of any of the properties, assets or facilities of the Company or (iii) arising out of, based upon, or resulting from the use of, any Proprietary Information or Third-Party Proprietary Information made available to me or to which I had access as an employee of the Company. Inventions assigned pursuant to this Section 2 to the Company, or to a third party as directed by

the Company pursuant to Section 2.5 below, are hereinafter referred to as "Company Inventions." At the request of the Company at any time and from time to time, I will execute and deliver any and all instruments, documents and agreements reasonably requested by the Company for purposes of confirming my assignment to the Company of all of my right, title and interest in and to any and all Company Inventions (and all Proprietary Rights with respect thereto), including, without limitation, at any time when any such Company Inventions (or any Proprietary Rights with respect thereto) are first reduced to practice or first fixed in a tangible medium, as applicable.

For the avoidance of doubt, notwithstanding any contrary provision contained herein, nothing contained in this Agreement shall require the assignment of any Invention (or Proprietary Right with respect thereto) made or conceived by me during the period of my employment to the extent such assignment is prohibited by any applicable state or federal law.

2.4 Obligation to Keep Company Informed. During the period of my employment with the Company and thereafter, I will promptly disclose to the Company fully and in writing all Company Inventions authored, conceived or reduced to practice by me, either alone or jointly with others. In addition, during the period of my employment with the Company and thereafter, I will promptly disclose to the Company all patent applications filed by me or on my behalf that claim any Company Invention.

2.5 Government or Third Party. I also agree to assign all my right, title and interest in and to any particular Company Invention to a third party, including without limitation the United States, as directed by the Company.

2.6 Works for Hire. I acknowledge that all original works of authorship which are made by me (solely or jointly with others) within the scope of my employment with the Company and which are protectable by copyright are "works made for hire," pursuant to the United States Copyright Act (17 U.S.C., Section 101).

2.7 Enforcement of Proprietary Rights. I will assist the Company in every proper way in obtaining, and from time to time enforcing, United States and foreign Proprietary Rights relating to Company Inventions in any and all countries. To that end I will promptly execute, verify and deliver such documents and perform such other acts (including appearances as a witness) as the Company may reasonably request for use in applying for, obtaining, perfecting, evidencing, sustaining and enforcing such Proprietary Rights and the assignment thereof. In addition, I will promptly execute, verify and deliver assignments of such Proprietary Rights to the Company or its designee. My obligation to assist the Company with respect to Proprietary Rights relating to such Company Inventions in any and all countries shall continue beyond the termination of my employment with the Company, but the Company shall compensate me at a reasonable rate after my termination for the time actually spent by me at the Company's request on such assistance.

In the event the Company is unable for any reason, after reasonable effort, to secure my signature on any document needed in connection with the actions specified in the preceding paragraph, I hereby irrevocably designate and appoint the Company and its duly authorized officers and agents as my agents and attorneys-in-fact, subject to full power or substitution and resubstitution, which appointment is coupled with an interest, to act for and in my behalf to execute, verify and file any such documents and to do all other lawfully permitted acts to further the purposes of the preceding paragraph with the same legal force and effect as if executed by me. I hereby waive and quitclaim

to the Company any and all claims, of any nature whatsoever, which I now or may hereafter have for infringement of any Proprietary Rights assigned hereunder to the Company.

3. RECORDS. I agree to keep and maintain adequate and current records (in the form of notes, memoranda, sketches, drawings and in any other form that may be required by the Company) of all Proprietary Information and all Company Inventions made, conceived, developed or reduced to practice by me, which records shall be available to and remain the sole property of the Company at all times.

4. NON-SOLICITATION. I agree that, during the period of my employment with the Company and for the one (1) year period after the date my employment with the Company ends for any reason, including but not limited to voluntary termination by me or termination by the Company, I will not, for myself or for the benefit of any other person (including, without limitation, any other person with which I may have a direct or indirect interest or relationship as an employee, consultant, advisor, equityholder or otherwise): (a) solicit, hire or engage, or attempt to solicit, hire or engage, any individual as an employee, consultant, advisor, officer, manager, managing partner, director or in any other similar capacity if such individual shall have been an employee of the Company or any of its subsidiaries or controlled affiliates at any time during the one (1) year period prior to the date of termination of my employment with the Company; (b) solicit, induce or attempt to induce any customer, vendor, contractor, consultant or advisor of the Company or any of its subsidiaries or controlled affiliates to terminate, diminish, or materially alter his, her or its relationship with the Company or any of its subsidiaries or controlled affiliates; or (c) solicit, induce or attempt to induce any potential customer, vendor, contractor, employee, consultant or advisor whose identity and potential relationship with the Company or any of its subsidiaries or controlled affiliates I learned as a result of my employment with the Company, not to establish, or to diminish or materially alter, such potential relationship with the Company or any of its subsidiaries or controlled affiliates. In the event that a court finds this Section 4, or any of its restrictions, to be unenforceable or invalid, I and the Company agree that (i) this Section 4 will be automatically modified to provide the Company with the maximum protection of its business interests allowed by law and (ii) I shall be bound, and such court shall enforce, this Section 4 as so modified.

5. NON-COMPETITION. I agree that, during the term of my employment with the Company and for the one (1) year period after the date my employment with the Company ends for any reason, including but not limited to voluntary termination by me or termination by the Company, I will not, directly or indirectly, as an officer, director, manager, employee, consultant, advisor, owner, partner, member, stockholder, or in any other capacity, (a) compete with the business or planned business of the Company or any of its subsidiaries or controlled affiliates, or (b) take any steps or actions to

facilitate or prepare for competition with the business or planned business of the Company or any of its subsidiaries or controlled affiliates, nor will I assist another person to take any action that I would be prohibited from taking under this Section 5. The obligations not to compete that I have undertaken under this Section 5 shall apply in all countries of the world. For purposes of this Section 5, I will not be deemed or treated as being in competition with the business or planned business of the Company or any of its subsidiaries or controlled affiliates or as being in violation of the covenant set forth in the clause (b) above in this Section 5 merely by virtue of my ownership of any equity interest in any business or person that is in competition with, or is planning to be in competition with, the business or planned business of the Company or any of its subsidiaries or controlled affiliates, if my ownership of any such equity interest represents

five percent (5%) or less the total equity interests in such business or person. I hereby acknowledge and agree that the foregoing restrictions contained in this Section 5 are reasonable, proper and necessitated by the legitimate business interests of the Company and will not prevent me from earning a living or pursuing my career. In the event that a court finds this Section 5, or any of its restrictions, to be unenforceable or invalid, I and the Company agree that (i) this Section 5 will be automatically modified to provide the Company with the maximum protection of its business interests allowed by law and (ii) I shall be bound, and such court shall enforce, this Section 5 as so modified. The parties agree that for the purposes of this Agreement, "business" shall mean development of MC4R agonists for the treatment of human disease.

6. NO CONFLICTING OBLIGATION. I represent that my performance of all the terms of this Agreement and as an employee of the Company has not breached, and does not and will not breach, any agreement to keep in confidence information acquired by me in confidence or in trust prior to, or outside the scope of, my employment by the Company and any agreement not to compete with the business of any third party. I have not entered into, and I agree I will not enter into, any agreement, either written or oral, in conflict herewith.

7. RETURN OF COMPANY DOCUMENTS. When I leave the employ of the Company, I will deliver to the Company any and all notes, memoranda, specifications, drawings, devices, formulas, and documents, together with all copies thereof, and any other material containing or disclosing any Company Inventions, Third Party Information or Proprietary Information of the Company. I further agree that, during the term of my employment with the Company or at any time thereafter, any property situated on the premises of the Company or any of its subsidiaries or controlled affiliates, including disks and other storage media, filing cabinets or other work areas, is subject to inspection by Company personnel at any time with or without notice. In the event I leave the employ of the Company for any reason whatsoever, I will promptly sign and deliver the "Termination Certificate" attached hereto as *Exhibit B*.

8. LEGAL AND EQUITABLE REMEDIES. Because my services are personal and unique and because I may have access to and become acquainted with the Proprietary Information of the Company, the Company shall have the right to enforce this Agreement and any of its provisions by injunction, specific performance, or other equitable relief, without bond and without prejudice to any other rights and remedies that the Company may have for a breach of this Agreement. In the event that the Company enforces the provisions of Section 4 or Section 5 hereof through a court order, I agree that the restrictions contained in Section 4 or Section 5, as the case may be, shall remain in effect for a period of one year from the effective date of such court order. I agree that if the Company is successful in whole or in part in any legal or equitable action against me under this Agreement, the Company shall be entitled to recover from me all costs, including reasonable attorney's fees, incurred by the Company in connection with such legal or equitable action.

9. NOTICES. Any notices required or permitted hereunder shall be given to the appropriate party at the address specified below or at such other address as the party shall specify in writing. Such notice shall be deemed given upon personal delivery to the appropriate address, one (1) business day after dispatch if sent by nationally recognized courier or overnight delivery service, on the date of dispatch if sent by facsimile or electronic mail for which confirmation of transmission is provided or, if sent by certified or registered mail, three (3) business days after the date of mailing.

10. NOTIFICATION OF NEW EMPLOYER. In the event that I leave the employ of the Company and accept new employment, I hereby agree to notify my new employer of my rights and obligations under this Agreement and I hereby consent to the Company or any person on behalf of the Company providing notice to my new employer of such rights and obligations.

11. GENERAL PROVISIONS

11.1 Governing Law; Consent to Personal Jurisdiction. This Agreement will be governed by and construed according to the laws of the Commonwealth of Massachusetts, as such laws are applied to agreements entered into and to be performed entirely within Massachusetts between Massachusetts residents. I hereby expressly consent to the personal jurisdiction of the state and federal courts located in the Commonwealth of Massachusetts for any lawsuit filed there against me by the Company arising from or related to this Agreement.

11.2 Severability. In case any one or more of the provisions contained in this Agreement shall, for any reason, be held to be invalid, illegal, or unenforceable in any respect, such invalidity, illegality, or unenforceability shall not affect the other provisions of this Agreement, and this Agreement shall be construed as if such invalid, illegal, or unenforceable provision had never been contained herein. Moreover, if any one or more of the provisions contained in this Agreement shall for any reason be held to be excessively broad as to duration, geographical scope, activity or subject, it shall be construed by limiting and reducing it, so as to be enforceable to the extent compatible with the applicable law as it shall then appear.

11.3 Successors and Assigns. This Agreement will be binding upon my heirs, executors, administrators and other legal representatives and will be for the benefit of the Company, its successors, and its assigns. Without limiting the generality of the foregoing, if I become an employee of any subsidiary or controlled affiliate of the Company, then (i) such subsidiary or controlled affiliate shall be deemed and treated as an intended third party beneficiary of this Agreement to the same extent as if such subsidiary or controlled affiliate were a party to this Agreement and (ii) each reference in this Agreement to the term "Company" shall be deemed to be a reference to whichever of Rhythm Pharmaceuticals, Inc. and/or such subsidiary, parent or controlled affiliate is my employer.

11.4 Survival. The provisions of this Agreement shall survive the termination of my employment with the Company and the assignment of this Agreement by the Company to any successor in interest or other assignee.

11.5 Employment. I agree and understand that nothing in this Agreement shall confer any right with respect to continuation of my employment by the Company, nor shall it interfere in any way with my right or the Company's right to terminate my employment at any time, with or without cause.

11.6 Waiver. No waiver by the Company of any breach of this Agreement shall be a waiver of any preceding or succeeding breach. No waiver by the Company of any right under this Agreement shall be construed as a waiver of any other right. The Company shall not be required to give notice to enforce strict adherence to all terms of this Agreement.

11.7 Entire Agreement. My obligations, and the Company's rights, under this Agreement shall apply to any time during which I was previously employed, or am in the future

employed, by the Company. This Agreement is the final, complete and exclusive agreement of the parties with respect to the subject matter hereof and supersedes all prior agreements relating to the subject matter hereof and merges all prior discussions between us. No modification of or amendment to this Agreement, nor any waiver of any rights under this Agreement, will be effective unless in writing and signed by the party to be charged. Any subsequent change or changes in my duties, salary or compensation will not affect the validity or scope of this Agreement.

11.8 Counterparts. This Agreement may be signed in counterparts, each shall be deemed an original and shall together constitute one agreement.

11.9 Acknowledgement. I acknowledge that this Agreement is a condition to my employment with the Company and that I have had a full and adequate opportunity to read, understand and discuss with my advisors, including legal counsel, the terms and conditions contained in this Agreement prior to signing hereunder.

This Agreement shall be effective as of the first day of my employment with the Company.

[Remainder of page intentionally left blank]

I HAVE READ THIS AGREEMENT CAREFULLY AND UNDERSTAND ITS TERMS. I HAVE COMPLETELY FILLED OUT EXHIBIT A TO THIS AGREEMENT.

Dated:

/s/ Nithya Desikan

Name: Nithya Desikan

Address: 82 Bay State Road, Belmont, MA 02478

ACCEPTED AND AGREED:

RHYTHM PHARMACEUTICALS, INC.

By: /s/ Keith Gottesdiener

Name: Keith Gottesdiener

Title: Chief Executive Officer

Dated:

EXHIBIT A

TO: Rhythm Pharmaceuticals, Inc.

FROM: Nithya Desikan

DATE: 7/24/17

SUBJECT: Prior Inventions

1. Except as listed in Section 2 below, the following is a complete list of all inventions or improvements relevant to the subject matter of my employment by Rhythm Pharmaceuticals, Inc. (the "Company") that have been made or conceived or first reduced to practice by me alone or jointly with others prior to my employment by the Company:

No inventions or improvements.

See below:

Additional sheets attached.

2. Due to a prior confidentiality agreement, I cannot complete the disclosure under Section 1 above with respect to inventions or improvements generally listed below, the proprietary rights and duty of confidentiality with respect to which I owe to the following party(ies):

Invention or Improvement	Party(ies)	Relationship
1.		
2.		
3.		

Additional sheets attached.

3. I acknowledge that this Exhibit A, if completed, forms a part of the Employee Proprietary Information, Inventions, Non-Competition and Non-Solicitation Agreement to which the Company and I are parties and that the failure to complete this Exhibit A and cause it to be attached to such Agreement constitutes a representation by me that I have no Prior Inventions.
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EXHIBIT B

TERMINATION CERTIFICATE

I hereby confirm and certify to the Company that I have returned to the Company all Proprietary Information in my possession or control, that I have disclosed fully to the Company all Company Inventions and that I have and will comply fully with all of my obligations to the Company under my Employee Proprietary Information, Inventions, Non-Competition and Non-Solicitation Agreement with the Company.

Name:

RHYTHM PHARMACEUTICALS, INC.

2015 EQUITY INCENTIVE PLAN

1. Definitions

As used in this 2015 Equity Incentive Plan, the following terms shall have the respective meanings set out below, unless the context clearly requires otherwise:

- 1.1. “Accelerate,” “Accelerated,” and “Acceleration,” when used with respect to an Option, means that as of the time of reference such Option will become exercisable with respect to some or all of the shares of Common Stock for which it was not then otherwise exercisable by its terms, and, when used with respect to any shares of Restricted Stock, means that as of the time of reference the Risk of Forfeiture otherwise still applicable to such shares of Restricted Stock shall expire or lapse.
 - 1.2. “Acquiring Person” means, with respect to any Transaction or any acquisition described in clause (ii) of the definition of Change of Control, the surviving or acquiring person or entity in connection with such Transaction or acquisition, as the case may be, *provided that* if such surviving or acquiring person or entity is controlled, directly or indirectly, by an Ultimate Parent Entity, the term “Acquiring Person” shall mean such Ultimate Parent Entity.
 - 1.3. “Affiliate” means, with respect to any person or entity, any other person or entity controlling, controlled by or under common control with the first person or entity.
 - 1.4. “Applicable Voting Control Percentage” means (i) at any time prior to the initial public offering of the Company, a percentage greater than fifty percent (50%) and (ii) at any time from and after the initial public offering of the Company, a percentage equal to or greater than twenty percent (20%).
 - 1.5. “Award” means any grant or sale pursuant to the Plan of Options, Restricted Stock or Stock Grants.
 - 1.6. “Award Agreement” means an agreement between the Company and the recipient of an Award, setting forth the terms and conditions of the Award.
 - 1.7. “Beneficial Ownership” has the meaning ascribed to such term in Rule 13d-3, or any successor rule thereto, promulgated by the Securities and Exchange Commission pursuant to the Exchange Act.
 - 1.8. “Board” means the Company’s board of directors.
 - 1.9. “Change of Control” means (i) the closing of any Sale of the Company Transaction or (ii) the direct or indirect acquisition, in a single transaction or a series of related transactions, by any person or Group (other than the Company or a Controlled Affiliate of the Company) of Beneficial Ownership of previously outstanding shares of capital stock of the Company if (A) immediately after such acquisition, such person or Group, together with their respective Affiliates, shall own or hold shares of capital stock of the Company possessing at least the Applicable Voting Control Percentage of the total combined voting power of all outstanding classes and/or series of capital stock of the Company and (B) immediately prior to such
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acquisition, such person or Group, together with their respective Affiliates, did not own or hold shares of capital stock of the Company possessing at least the Applicable Voting Control Percentage of the total combined voting power of all outstanding classes and/or series of capital stock of the Company. Notwithstanding anything expressed or implied in the foregoing provisions of this definition to the contrary, any direct or indirect acquisition referred to in clause (ii) above in this definition shall not be treated as a Change of Control if, at any time prior to or after such direct or indirect acquisition, a majority of the members of the Board as constituted immediately prior to such direct or indirect acquisition consent in writing to exclude such direct or indirect acquisition from the scope of this definition.

1.10. “Code” means the Internal Revenue Code of 1986, as amended from time to time, or any successor statute thereto, and any regulations issued from time to time thereunder.

- 1.11. “Controlled Affiliate” means, with respect to any person or entity, any other person or entity that is controlled by such person or entity.
- 1.12. “Committee” means any committee of the Board delegated responsibility by the Board for the administration of the Plan, as provided in Section 5 of the Plan. For any period during which no such committee is in existence, the term “Committee” shall mean the Board and all authority and responsibility assigned the Committee under the Plan shall be exercised, if at all, by the Board.
- 1.13. “Common Stock” means common stock, par value \$0.001 per share, of the Company.
- 1.14. “Company” means Rhythm Pharmaceuticals, Inc., a corporation organized under the laws of the State of Delaware.
- 1.15. “Grant Date” means the date as of which an Option is granted, as determined under Section 7.1(a).
- 1.16. “Exchange Act” means the Securities and Exchange Act of 1934, as amended.
- 1.17. “Group” has the meaning ascribed to such term in Section 13(d)(3) of the Exchange Act or any successor section thereto.
- 1.18. “Incentive Option” means an Option that by its terms is to be treated as an “incentive stock option” within the meaning of Section 422 of the Code.
- 1.19. “Market Value” means the fair market value of a share of Common Stock on a particular date as determined by the Committee.

- 1.20. “Non-statutory Option” means any Option that is not an Incentive Option.
- 1.21. “Option” means an option granted under the Plan to purchase shares of Common Stock.
- 1.22. “Optionee” means an employee, consultant, officer or director of the Company to whom an Option shall have been granted under the Plan.

1.23. “Participant” means any holder of an outstanding Award under the Plan or any holder of shares of Common Stock issued upon exercise of any Option.

1.24. “Plan” means this 2015 Equity Incentive Plan of the Company, as amended and in effect from time to time, and including any attachments or addenda hereto.

1.25. “Restricted Stock” means a grant or sale of shares of Common Stock pursuant to the Plan to an employee, consultant, officer or director of the Company if and to the extent that such grant or sale of such shares of Common Stock is made subject to a Risk of Forfeiture.

1.26. “Restriction Period” means the period of time, established by the Committee in connection with an Award of shares of Restricted Stock, during which such shares of Restricted Stock are subject to a Risk of Forfeiture described in the applicable Award Agreement.

1.27. “Risk of Forfeiture” means a limitation on the right of a Participant to retain an Award of Restricted Stock arising because of the occurrence or non-occurrence of specified events or conditions described in the applicable Award Agreement, including, but not limited to, a limitation on the right of a Participant to retain an Award of Restricted Stock by virtue of any right granted or retained by the Company to reacquire all or any portion of such Restricted Stock upon termination of the employment, consulting relationship, officer status or Board membership, as the case may be, with the Company or any of its Affiliates of the person to whom such Award of Restricted Stock was originally made and regardless of whether such reacquisition is at a purchase price less than, equal to, or greater than the Market Value of the Restricted Stock at the time of such reacquisition.

1.28. “Sale of the Company Transaction” means any Transaction in which the stockholders of the Company immediately prior to such Transaction, together with any and all of such stockholders’ Affiliates, do not own or hold, immediately after consummation of such Transaction, shares of capital stock of the Acquiring Person in connection with such Transaction possessing at least a majority of the total voting power of the outstanding capital stock of such Acquiring Person.

1.29. “Securities Act” means the Securities Act of 1933, as amended.

1.30. “Stock Grant” a grant or sale of shares of Common Stock pursuant to the Plan to an employee, consultant, officer or director of the Company if and to the extent that such grant or sale of such shares of Common Stock is made free from any Risk of Forfeiture.

1.31. “Stockholder Agreement” means one agreement, or, collectively, two or more agreements, as may be amended from time to time, by and among the Company and one or more stockholders of the Company (including, without limitation, any Participant or prospective Participant that became a stockholder of the Company as a result of the receipt, transfer or exercise of any Award) setting forth, among other provisions, restrictions on transfer, rights of first refusal, lock-up arrangements, bring-along rights, drag-along rights, voting agreements or the granting of certain proxies or powers of attorney with respect to shares of capital stock. Any and all provisions of this Plan that apply to any Stockholder Agreement shall be deemed to be applicable to any such agreement or agreements referred to in this definition even if such agreement or agreements are called or titled something other than Stockholder Agreement or Stockholders Agreement.

1.32. “Ten Percent Owner” means a person who owns, or is deemed within the meaning of Section 422(b)(6) of the Code to own, stock possessing more than 10% of the total combined voting power of all classes of stock of the Company (or any parent or subsidiary corporations of the Company, as defined in Section 424(e) and (f), respectively, of the Code). Whether a person is a Ten Percent Owner shall be determined with respect to each Option based on the facts existing immediately prior to the Grant Date of such Option.

1.33. “Transaction” means any merger or consolidation of the Company with or into another person or entity or the sale or transfer of all or substantially all of the assets of the Company, in each case in a single transaction or in a series of related transactions.

1.34. “Ultimate Parent Entity” shall mean, with respect to any Person that is not an individual, any other Person that (i) directly or indirectly controls such Person and (ii) is not itself controlled, directly or indirectly, by one or more Persons that are not individuals.

2. Purpose

This Plan is intended to encourage ownership of Common Stock by employees, consultants, officers and directors of the Company and its Affiliates and to provide additional incentive for them to promote the success of the Company’s business. The Plan is intended to be an incentive stock option plan within the meaning of Section 422 of the Code but not all Awards granted hereunder are required to be Incentive Options.

3. Term of the Plan

Unless the Plan shall have been earlier terminated by the Board, Awards may be granted under this Plan at any time in the period commencing upon the date of approval of the Plan by the Board and ending immediately prior to the tenth anniversary of the earlier of the adoption of the Plan by the Board and the approval of the Plan by the Company’s stockholders. Awards granted pursuant to the Plan within such period shall not expire solely by reason of the termination of the Plan. Awards of Incentive Options granted prior to stockholder approval of the Plan are hereby expressly conditioned upon such approval, but in the event of the failure of the stockholders to approve the Plan shall thereafter and for all purposes be deemed to constitute Non-statutory Options.

4. Stock Subject to the Plan

Subject to adjustment as provided in Section 8.1, at no time shall the number of shares of Common Stock issued pursuant to or subject to outstanding Awards under the Plan (including, without limitation, pursuant to Incentive Options) exceed twenty-one million two hundred fifty thousand (21,250,000) shares of Common Stock. For purposes of applying the foregoing limitation, (a) if any Option expires, terminates, or is cancelled for any reason without having been exercised in full, or if any Award of Restricted Stock is forfeited by a Participant, the shares of Common Stock not purchased upon exercise of such Option and/or any such Award of Restricted Stock so forfeited shall again be available for Awards thereafter to be granted under the Plan, and (b) if any Option is exercised by delivering previously owned shares of Common Stock in payment of the exercise price therefor, only the net number of shares, that is, the number of shares issued minus the number received by the Company in payment of the exercise price, shall be considered to have been issued pursuant to an Award granted under the Plan. Shares of Common Stock issued pursuant to the Plan may be either authorized but unissued shares or shares held by the Company in its treasury.

5. Administration

The Plan shall be administered by the Committee; *provided, however,* that at any time and on any one or more occasions the Board may itself exercise any of the powers and responsibilities assigned the Committee under the Plan and when so acting shall have the benefit of all of the provisions of the Plan pertaining to the Committee's exercise of its authorities hereunder; *and provided further* that the Committee may delegate to an executive officer or officers the authority to grant Awards hereunder to employees who are not officers, and to consultants, in accordance with such guidelines as the Committee shall set forth at any time or from time to time. Subject to the provisions of the Plan, the Committee shall have complete authority, in its discretion, to make or to select the manner of making all determinations with respect to each Award to be granted by the Company under the Plan in addition to any other determination allowed the Committee under the Plan including, without limitation: (a) the employee, consultant, officer or director to receive the Award; (b) the form of Award; (c) whether an Option (if granted to an employee) will be an Incentive Option or a Non-statutory Option; (d) the time of granting an Award; (e) the number of shares subject to an Award; (f) the exercise price of an Option or purchase price, if any, for shares of Restricted Stock or for a Stock Grant and the method of payment of such exercise price or such purchase price; (g) the term of an Option; (h) the Restricted Period and the Risk of Forfeiture applicable to any Award of Restricted Stock as well as the Acceleration, if any, of such Restricted Period and Risk of Forfeiture; (i) the exercise date or dates of an Option as well as the Acceleration, if any, of such exercise date or dates; and (j) the effect of termination of any employment, consulting, officership or Board member relationship with the Company or any of its Affiliates on the subsequent exercisability of an Option or on the Risk of Forfeiture of Restricted Stock. In making such determinations, the Committee may take into account the nature of the services rendered by the respective employees, consultants, officers and directors, their present and potential contributions to the success of the Company and its Affiliates, and such other factors as the Committee in its discretion shall deem relevant. Subject to the provisions of the Plan, the Committee shall also have complete authority to interpret the Plan, to prescribe, amend and rescind rules and regulations relating to it, to determine the terms and provisions of the respective Award Agreements (which need not be identical), and to make all other determinations necessary or advisable for the administration of the Plan. The Committee's determinations made in good faith on matters referred to in this Plan shall be final, binding and conclusive on all persons having or claiming any interest under the Plan or an Award made pursuant hereto.

6. Authorization and Eligibility

The Committee may grant from time to time and at any time prior to the termination of the Plan one or more Awards, either alone or in combination with any other Awards, to any employee of, or consultant to, one or more of the Company and its Affiliates or to any non-employee officer or member of the Board or of any board of directors (or similar governing authority) of any Affiliate. However, only employees of the Company or of any parent or subsidiary corporations of the Company, as defined in Sections 424(e) and (f), respectively, of the Code, shall be eligible for the grant of an Incentive Option.

Each grant of an Award shall be subject to all applicable terms and conditions of the Plan (including but not limited to any specific terms and conditions applicable to that type of Award set out in Section 7 below), and such other terms and conditions, not inconsistent with the terms of the Plan, as the Committee may prescribe. No prospective Participant shall have any rights with respect to an Award, unless and until such Participant has executed an agreement evidencing

the Award (or the transfer thereof to such Participant), delivered a fully executed copy thereof to the Company, and otherwise complied with the applicable terms and conditions of such Award.

7. Specific Terms of Awards

7.1 Options.

(a) **Date of Grant.** The granting of an Option shall take place at the time specified in the Award Agreement. Only if expressly so provided in the applicable Award Agreement shall the Grant Date be the date on which the Award Agreement shall have been duly executed and delivered by the Company and the Optionee.

(b) **Exercise Price.** The price at which shares of Common Stock may be acquired under each Incentive Option shall be not less than 100% of the Market Value of Common Stock on the Grant Date, or not less than 110% of the Market Value of Common Stock on the Grant Date if the Optionee is a Ten Percent Owner. The price at which shares may be acquired under each Non-statutory Option shall not be so limited solely by reason of this Section.

(c) **Option Period.** No Incentive Option may be exercised on or after the tenth anniversary of the Grant Date, or on or after the fifth anniversary of the Grant Date if the Optionee is a Ten Percent Owner. The Option period under each Non-statutory Option shall not be so limited solely by reason of this Section.

(d) **Exercisability.** An Option may be immediately exercisable or become exercisable in such installments, cumulative or non-cumulative, as the Committee may determine. In the case of an Option not otherwise immediately exercisable in full, the Committee may Accelerate such Option in whole or in part at any time; *provided, however,* that in the case of an Incentive Option, any such Acceleration of such Incentive Option would not cause such Incentive Option to fail to comply with the provisions of Section 422 of the Code or the Optionee consents to such Acceleration.

(e) **Effect of Termination of Employment, Consulting, Officer or Board Member Relationship.** Unless the Committee shall provide otherwise with respect to any Option, if the applicable Optionee's association with the Company or any of its Affiliates as an employee, consultant, officer or director ends for any reason or no reason, regardless of whether the end of such association is effected by the Company, any such Affiliate or such Optionee (whether voluntarily or involuntarily, including because an entity with which such Optionee has any such association ceases to be an Affiliate of the Company), and immediately following the end of any such association, such Optionee is not associated with the Company or any of its Affiliates as an employee, consultant, officer or director, or if such Optionee dies, then any outstanding Option initially granted to such Optionee, whether then held by such Optionee or any other Participant, shall cease to be exercisable in any respect and shall terminate on the ninetieth (90th) day following the end of such association or such death and, for the period it remains exercisable following the end of such association or such death, shall be exercisable only to the extent exercisable on the date of the end of such association or such death. Military or sick leave or other bona fide leave shall not be deemed a termination of employment, *provided that* it does not exceed the longer of ninety (90) days or the period during which the absent Optionee's reemployment rights, if any, are guaranteed by statute or by contract.

(f) **Transferability.** Except as otherwise provided in this subsection (f), Options shall not be transferable, and no Option or interest therein may be sold, transferred, pledged, assigned, or otherwise alienated or hypothecated, other than by will or by the laws of descent and distribution (subject always to the provisions of subsection (e) above). Except as otherwise provided in this subsection (f), all of a Participant's rights in any Option may be exercised during the life of such Participant only by such Participant or such Participant's legal representative. The Committee may (at or after the grant of a Non-statutory Option) provide that a Non-statutory Option may be transferred by the applicable Participant to a family member; *provided, however,* that any such transfer is without payment of any consideration whatsoever and that no transfer of a Non-statutory Option shall be valid unless first approved by the Committee, acting in its sole discretion, unless such transfer is permitted under the applicable Award Agreement. For this purpose, "family member" means any child, stepchild, grandchild, parent, stepparent, spouse, former spouse, sibling, niece, nephew, mother-in-law, father-in-law, son-in-law, daughter-in-law, brother-in-law, or sister-in-law, including adoptive relationships, any person sharing the applicable Participant's household (other than a tenant or employee), a trust in which the foregoing persons and/or the applicable Participant have more than fifty percent (50%) of the beneficial interests, a foundation in which the foregoing persons and/or the applicable Participant control the management of assets, and any other entity in which these persons and/or the applicable Participant own more than fifty percent (50%) of the voting interests. The Committee may at any time or from time to time delegate to one or more officers of the Company the authority to permit transfers of Non-statutory Options to third parties pursuant to this subsection (f), which authorization shall be exercised by such officer or officers in accordance with guidelines established by any Committee at any time and from time to time.

(g) **Method of Exercise.** An Option may be exercised by a Participant giving written notice, in the manner provided in Section 15, specifying the number of shares of Common Stock with respect to which the Option is then being exercised. The notice shall be accompanied by payment in the form of cash or check payable to the order of the Company in an amount equal to the exercise price of the shares of Common Stock to be purchased or, subject in each instance to the Committee's approval, acting in its sole discretion and subject to such conditions, if any, as the Committee may deem necessary to comply with applicable laws, rules and regulations or to avoid adverse accounting effects to the Company, by delivery to the Company of (i) shares of Common Stock having a Market Value equal to the exercise price of the shares to be purchased, or (ii) the Participant's executed promissory note in the principal amount equal to the exercise price of the shares to be purchased and otherwise in such form as the Committee shall have approved. Receipt by the Company of such notice and payment in any authorized or combination of authorized means shall constitute the exercise of the Option. Within thirty (30) days thereafter but subject to the remaining provisions of the Plan, the Company shall deliver or cause to be delivered to the Participant or his agent a certificate or certificates for the number of shares then being purchased. Such shares shall be fully paid and nonassessable. Notwithstanding any of the foregoing provisions in this subsection (g) to the contrary, (A) no Option shall be considered to have been exercised unless and until all of the provisions governing such exercise specified in the Plan and in the relevant Award Agreement shall have been duly complied with; and (B) the obligation of the Company to issue any shares upon exercise of an Option is subject to all of the applicable provisions of Section 9 hereof and to compliance by the applicable Optionee and the applicable Participant that is the then holder of such Option with all of the provisions of the Plan and the relevant Award Agreement.

(h) **Limit on Incentive Option Characterization.** An Incentive Option shall be considered to be an Incentive Option only to the extent that the number of shares of Common

Stock for which the Option first becomes exercisable in a calendar year do not have an aggregate Market Value (as of the date of the grant of the Option) in excess of the "current limit". The current limit for any Optionee for any calendar year shall be \$100,000 minus the aggregate Market Value at the date of grant of the number of shares of Common Stock available for purchase for the first time in the same year under each other Incentive Option previously granted to the Optionee under the Plan, and under each other incentive stock option previously granted to the Optionee under any other incentive stock option plan of the Company and its Affiliates, after December 31, 1986. Any shares of Common Stock which would cause the foregoing limit to be violated shall be deemed to have been granted under a separate Non-statutory Option, otherwise identical in its terms to those of the Incentive Option.

(i) **Notification of Disposition.** Each person exercising any Incentive Option granted under the Plan shall be deemed to have covenanted with the Company to report to the Company any disposition of such shares prior to the expiration of the holding periods specified by Section 422(a)(1) of the Code and, if and to the extent that the realization of income in such a disposition imposes upon the Company federal, state, local or other withholding tax requirements, or any such withholding is required to secure for the Company an otherwise available tax deduction, to remit to the Company an amount in cash sufficient to satisfy those requirements.

(j) **Rights Pending Exercise.** No person holding an Option shall be deemed for any purpose to be a stockholder of the Company with respect to any of the shares of Common Stock issuable pursuant to such Option, except to the extent that such Option shall have been exercised with respect thereto and, in addition, a certificate shall have been issued therefor and delivered to such person or his agent.

(a) Purchase Price. Shares of Restricted Stock shall be issued under the Plan for such consideration, in cash, other property or services, or any combination thereof, as is determined by the Committee.

(b) Issuance of Certificates. Subject to subsection (c) below, each Participant receiving an Award of Restricted Stock shall be issued a stock certificate in respect of such shares of Restricted Stock. Such certificate shall be registered in the name of such Participant, and, if applicable, shall bear an appropriate legend referring to the terms, conditions, and restrictions applicable to such Award substantially in the following form:

The transferability of this certificate and the shares represented by this certificate are subject to the terms and conditions of the Rhythm Pharmaceuticals, Inc. 2015 Equity Incentive Plan and an Award Agreement entered into by the record owner of such shares and Rhythm Pharmaceuticals, Inc., in each case as the same may be amended. Copies of such Plan and Award Agreement are on file in the offices of Rhythm Pharmaceuticals, Inc.

(c) Escrow of Shares. The Committee may require that the stock certificates evidencing shares of Restricted Stock be held in custody by a designated escrow agent (which may but need not be the Company) until the restrictions thereon shall have lapsed, and that the Participant deliver a stock power, endorsed in blank, relating to the Common Stock covered by such Award.

(d) Restrictions and Restriction Period. During the Restriction Period applicable to shares of Restricted Stock, such shares shall be subject to limitations on transferability and a Risk of Forfeiture arising on the basis of such conditions related to the performance of services, Company or Affiliate performance or otherwise as the Committee may determine and provide for in the applicable Award Agreement. Any such Risk of Forfeiture may be waived or terminated, or the Restriction Period shortened, at any time by the Committee on such basis as it deems appropriate.

(e) Rights Pending Lapse of Risk of Forfeiture or Forfeiture of Award. Except as otherwise provided in the Plan or the applicable Award Agreement, at all times prior to lapse of any Risk of Forfeiture applicable to, or forfeiture of, an Award of Restricted Stock, the applicable Participant shall have all of the rights of a stockholder of the Company, including the right to vote the shares of Restricted Stock.

(f) Effect of Termination of Employment, Consulting, Officer or Board Member Relationship. Unless otherwise determined by the Committee at or after an Award of Restricted Stock is made by the Company to any Participant and subject to the applicable provisions of the Award Agreement, if such Participant's association with the Company or any of its Affiliates as an employee, consultant, officer or director ends for any reason or no reason during the Restriction Period, regardless of whether the end of such association is effected by the Company, any such Affiliate or such Participant (whether voluntarily or involuntarily, including because an entity with which such Participant has any such association ceases to be an Affiliate of the Company), and immediately following the end of any such association, such Participant is not associated with the Company or any of its Affiliates as an employee, consultant, officer or director, or if such Participant dies, then all outstanding shares of Restricted Stock initially awarded or sold to such Participant that are still subject to Risk of Forfeiture, whether then held by such Participant or any other Participant that is the direct or indirect transferee of such Participant, shall be forfeited or otherwise subject to return to or repurchase by the Company if and to the extent so provided by, and subject to and in accordance with, the terms of the applicable Award Agreement; *provided, however,* that military or sick leave or other bona fide leave shall not be deemed a termination of employment, if it does not exceed the longer of ninety (90) days or the period during which the absent Participant's rights, if any, are guaranteed by statute or by contract.

(g) Lapse of Restrictions. If and when the Restriction Period expires without a prior forfeiture of the Restricted Stock, the certificates for such shares shall be delivered to the Participant promptly if not theretofore so delivered.

(h) Transferability. Except as otherwise provided in this subsection (h), shares of Restricted Stock shall not be transferable during the applicable Restriction Period, and no share of Restricted Stock or interest therein may be sold, transferred, pledged, assigned, or otherwise alienated or hypothecated during the applicable Restriction Period, other than by will or by the laws of descent and distribution (subject always to the provisions of subsection (f) above). The applicable Award Agreement or the Committee (at or after the grant of a share of Restricted Stock) may provide that such share of Restricted Stock may be transferred by the applicable Participant to a family member during the applicable Restriction Period; *provided, however,* that any such transfer is without payment of any consideration whatsoever and that no transfer of a share of Restricted Stock during the applicable Restriction Period shall be valid unless first approved by the Committee, acting in its sole discretion, unless such transfer is permitted under the applicable Award Agreement. For this purpose, "family member" means any child, stepchild,

grandchild, parent, stepparent, spouse, former spouse, sibling, niece, nephew, mother-in-law, father-in-law, son-in-law, daughter-in-law, brother-in-law, or sister-in-law, including adoptive relationships, any person sharing the applicable Participant's household (other than a tenant or employee), a trust in which the foregoing persons and/or the applicable Participant have more than fifty percent (50%) of the beneficial interests, a foundation in which the foregoing persons and/or the applicable Participant control the management of assets, and any other entity in which these persons and/or the applicable Participant own more than fifty percent (50%) of the voting interests. The Committee may at any time or from time to time delegate to one or more officers of the Company the authority to permit transfers of shares of Restricted Stock during the applicable Restriction Period to third parties pursuant to this subsection (h), which authorization shall be exercised by such officer or officers in accordance with guidelines established by the Committee at any time and from time to time.

7.3 Stock Grants.

(a) In General. Stock Grants shall be issued for such consideration, in cash, other property or services, or any combination thereof, as is determined by the Committee. Without limiting the generality of the foregoing, Stock Grants may be awarded in such circumstances as the Committee deems appropriate, including without limitation in recognition of significant contributions to the success of the Company or its Affiliates or in lieu of compensation otherwise already due. Stock Grants shall be made without forfeiture conditions of any kind.

(b) Issuance of Certificates. Each Participant receiving a Stock Grant shall be issued a stock certificate in respect of such Stock Grant. Such certificate shall be registered in the name of such Participant, and, if applicable, shall bear an appropriate legend referring to the terms,

conditions, and restrictions applicable to such Award substantially in the following form:

The transferability of this certificate and the shares represented by this certificate are subject to the terms and conditions of the Rhythm Pharmaceuticals, Inc. 2015 Equity Incentive Plan, as the same may be amended. A copy of such Plan is on file in the offices of Rhythm Pharmaceuticals, Inc.

7.4 Awards to Participants Outside the United States. The Committee may modify the terms of any Award under the Plan if the applicable Participant is, at the time of grant or award of such Award to such Participant or, if such Award is not initially granted or awarded to such Participant, at the time such Participant first acquires rights or any interest in such Award or at any time during the term of such Award, resident or primarily employed outside of the United States in any manner deemed by the Committee to be necessary or appropriate in order that such Award shall conform to laws, regulations, and customs of the country in which such Participant is then resident or primarily employed, or so that the value and other benefits of such Award to such Participant, as affected by foreign tax laws and other restrictions applicable as a result of such Participant's residence or employment abroad, shall be comparable to the value of such an Award to a Participant who is resident or primarily employed in the United States. An Award may be modified under this Section 7.4 in a manner that is inconsistent with the express terms of the Plan, so long as such modifications will not contravene any applicable law or regulation. The Committee may establish supplements to, or amendments, restatements, or alternative versions of the Plan for the purpose of granting and administrating any such modified Award. No such modification, supplement, amendment, restatement or alternative version may increase the share limit of Section 4.

8. Adjustment Provisions

8.1 Adjustment for Corporate Actions. Subject to the provisions of Section 8.2, if at any time or from time to time after the date on which the Board has adopted this Plan, the outstanding shares of Common Stock (or any other securities covered by the Plan by reason of the prior application of this Section 8.1) are increased, decreased, or exchanged for a different number or kind of shares or other securities, or if additional shares or new or different shares or other securities are distributed with respect to such shares of Common Stock or other securities, through merger, consolidation, sale of all or substantially all the property of the Company, reorganization, recapitalization, reclassification, stock dividend, stock split, reverse stock split, or other distribution with respect to such shares of Common Stock, or other securities, an appropriate and proportionate adjustment will be made in (i) the maximum numbers and kinds of shares provided in Section 4, (ii) the numbers and kinds of shares or other securities subject to the then outstanding Awards, (iii) the exercise price for each share or other unit of any other securities subject to then outstanding Options (without change in the aggregate purchase price as to which such Options remain exercisable), and (iv) the repurchase price of each share of Restricted Stock then subject to a Risk of Forfeiture in the form of a Company repurchase right.

8.2 Change of Control. Subject to the applicable provisions of the Award Agreement, in the event of a Change of Control, the Committee shall have the discretion, exercisable in advance of, at the time of, or (except to the extent otherwise provided below) at any time after, the Change of Control, to provide for any or all of the following (subject to and upon such terms as the Committee may deem appropriate): (A) the Acceleration, in whole or in part, of any or all outstanding Options (including Options that are assumed or replaced pursuant to clause (C) below) that are not exercisable in full at the time the Change of Control, such Acceleration to become effective at the time of the Change of Control, or at such time following the Change of Control that the employment, consulting, officer or Board member relationship of the applicable Optionee or Optionees (or of the Participant that is the then holder of any such Option) with the Company and its Affiliates (including, without limitation, the Acquiring Person or any of its Affiliates) terminates, or at such other time or times as the Committee shall determine; (B) the lapse or termination of the Risk of Forfeiture (including, without limitation, all or any (or any portion) of the Company's repurchase rights) with respect to outstanding Awards of Restricted Stock, such lapse or termination to become effective at the time of the Change of Control, or at such time following the Change of Control that the employment, consulting, officer or Board member relationship with the Company and its Affiliates (including, without limitation, the Acquiring Person or any of its Affiliates) of the Participant or Participants that hold such Awards of Restricted Stock (or the person to whom such Awards of Restricted Stock were initially made) terminates, or at such other time or times as the Committee shall determine; (C) the assumption of all or any (or any portion of) outstanding Options, or the substitution of all or any (or any portion of) outstanding Options with equivalent options, by the Acquiring Person or any of its Affiliates; or (D) the termination of all or any (or any portion of) Options (other than Options that are assumed or substituted pursuant to clause (C) above) that remain outstanding at the time of the consummation of the Change of Control, *provided that*, the Committee shall have made the determination to effect such termination prior to the consummation of the Change of Control and there has been or there will be full compliance with any applicable provisions set forth below in this Section 8.2 that may require in certain cases or under certain circumstances the payment of or provision of consideration to holders of Options terminated pursuant to the provisions of this clause (D), and *provided, further, that*, subject to and without limiting the provisions set forth in the next sentence, if the Committee shall have determined in its sole and absolute discretion that the Company make payment or provide consideration to the holders of such terminated Options

on account of such termination, which payment or consideration shall be on such terms and conditions as the Committee shall have determined, then the Company shall be required to make such payment or provide such consideration in accordance with the terms and conditions so determined by the Committee; otherwise, except if and to the extent otherwise provided in the next sentence, the Company shall not be required to make any payment or provide any consideration in connection with, or as a result of, the termination of Options pursuant to the foregoing provisions of this clause (D). Notwithstanding anything express or implied in the foregoing provisions of this Section 8.2 to the contrary, in the event that the Committee elects, in its sole and absolute discretion, to terminate all or any (or any portion of) Options pursuant to the provisions of the foregoing clause (D) and the Committee does not provide to any Participant that is a holder of an Option any portion of which is both exercisable immediately prior to the applicable Change of Control and to be terminated pursuant to the provisions of the foregoing clause (D) (each, a "Terminated Vested Option") at least five (5) business days prior written notice of such potential termination thereof, then, prior to the consummation of such applicable Change of Control, the Committee shall ensure that adequate provision has been made so that the Company, the Acquiring Person or any of their respective Affiliates is legally obligated to make payment or provide consideration on account of such termination to such holder of such Terminated Vested Option that was not provided such prior written notice of termination, which payment or consideration shall consist of the difference between (x) the cash, stock, securities, other property or other consideration that would have been received in connection with such applicable Change of Control by such holder of such Terminated Vested Option that was not provided such prior written notice of termination if such holder had exercised such Terminated Vested Option immediately prior to such applicable Change of Control (or cash, stock, securities, other property or other consideration having a fair market value (as determined by the Committee in good faith) equal to the cash, stock, securities, other property or other consideration to which such holder of such Terminated Vested Option would otherwise be entitled under this clause (x)) and (y) the aggregate exercise price with respect to such Terminated Vested Option. The provisions of this Section 8.2 shall not be construed as to limit or restrict in any

way the Committee's general authority under Sections 7.1(d) or 7.2(d) hereof to Accelerate Options in whole or in part at any time or to waive or terminate at any time any Risk of Forfeiture applicable to shares of Restricted Stock. Each outstanding Option, or portion thereof, that is assumed in connection with a Change of Control, or is otherwise to continue in effect subsequent to a Change of Control, will be appropriately adjusted, immediately after the Change of Control, as to the number and class of securities and the price at which it may be exercised in accordance with Section 8.1.

8.3 Dissolution or Liquidation. Upon dissolution or liquidation of the Company, each outstanding Option shall terminate, but each Participant shall have the right, immediately prior to such dissolution or liquidation, to exercise any and all Options held by such Participant to the extent such Options are exercisable on the date of such dissolution or liquidation.

8.4 Related Matters. Any adjustment in Awards made pursuant to this Section 8 shall be determined and made, if at all, by the Committee and shall include any correlative modification of terms, including exercise prices, rates of vesting or exercisability, Risks of Forfeiture and applicable repurchase prices, which the Committee may deem necessary or appropriate so as to ensure that the rights of the Participants in their respective Awards are not substantially diminished nor enlarged as a result of the adjustment and corporate action other than as expressly contemplated in this Section 8. No fraction of a share shall be purchasable or deliverable upon exercise, but in the event any adjustment hereunder of the number of shares covered by an Award shall cause such number to include a fraction of a share, such number of

shares shall be adjusted to the nearest smaller whole number of shares. No adjustment of an Option exercise price per share pursuant to this Section 8 shall result in an exercise price that is less than the par value of the Common Stock.

9. Settlement of Awards

9.1 Violation of Law. Notwithstanding any other provision of the Plan or the relevant Award Agreement, if, at any time, in the reasonable opinion of the Company, the issuance of shares of Common Stock covered by an Award may constitute a violation of law, then the Company may delay such issuance and the delivery of a certificate for such shares until (i) approval shall have been obtained from such governmental agencies, other than the Securities and Exchange Commission, as may be required under any applicable law, rule, or regulation and (ii) in the case where such issuance would constitute a violation of a law administered by or a regulation of the Securities and Exchange Commission, one of the following conditions shall have been satisfied:

- (a) the shares are at the time of the issue of such shares effectively registered under the Securities Act; or
- (b) the Company shall have determined, on such basis as it deems appropriate (including an opinion of counsel in form and substance satisfactory to the Company) that the sale or issuance of such shares does not require registration under the Securities Act or any applicable state securities laws.

9.2 Corporate Restrictions on Rights in Stock. Any Common Stock to be issued pursuant to Awards shall be subject to all restrictions upon the transfer thereof that may be now or hereafter imposed by the Certificate of Incorporation and the By-laws of the Company, each as amended and in effect from time to time. Whenever Common Stock is to be issued pursuant to an Award, if the Committee so directs at the time of the grant (or, if such Award is an Option, at any time prior to the exercise thereof), the Company shall be under no obligation, notwithstanding any other provision of the Plan or the relevant Award Agreement to the contrary, to issue such Common Stock until such time, if ever, as the applicable Participant or prospective Participant shall have become a party to and bound by any agreement (including, without limitation, any Stockholder Agreement) that the Committee, in its sole discretion, shall require that such Participant or prospective Participant enter into prior to, and as a condition to, the issuance of such Common Stock by the Company to such Participant or prospective Participant.

9.3 Investment Representations. The Company shall be under no obligation to issue any shares covered by an Award unless such have been effectively registered under the Securities Act or the Participant shall have made such written representations to the Company (and upon which the Company believes it may reasonably rely) as the Company may deem necessary or appropriate for purposes of confirming that the issuance of such shares will be exempt from the registration requirements of that Act and any applicable state securities laws and otherwise in compliance with all applicable laws, rules and regulations, including but not limited to that the Participant is acquiring shares for his or her own account for the purpose of investment and not with a view to, or for sale in connection with, the distribution of any such shares.

9.4 Registration. If the Company shall deem it necessary or desirable to register under the Securities Act or other applicable statutes any shares of Common Stock issued or to be issued pursuant to Awards, or to qualify any such shares of Common Stock for exemption from

the Securities Act or other applicable statutes, then the Company shall take such action at its own expense. The Company may require from each recipient of an Award, or each holder of shares of Common Stock acquired pursuant to the Plan, such information in writing for use in any registration statement, prospectus, preliminary prospectus or offering circular as is reasonably necessary for such purpose and may require reasonable indemnity to the Company and its officers and directors from such holder against all losses, claims, damage and liabilities arising from such use of the information so furnished and caused by any untrue statement of any material fact therein or caused by the omission to state a material fact required to be stated therein or necessary to make the statements therein not misleading in the light of the circumstances under which they were made.

9.5 Lock-Up. If, in connection with any underwritten public offering of securities of the Company, the Company sends written notice to each Participant stating that the restrictions on transfer set forth in this Section 9.5 are applicable to such underwritten public offering, no Participant shall sell, make any short sale of, loan, grant any option for the purchase of, pledge or otherwise encumber, or otherwise dispose of, any shares of Common Stock or any Awards during the one hundred-eighty (180) day period (and which period may be extended as requested by the Company or an underwriter to accommodate regulatory restrictions on (1) the publication or other distribution of research reports and (2) analyst recommendations and opinions, including, but not limited to, the restrictions contained in FINRA Rule 2711(f)(4) or NYSE Rule 472(f)(4), or any successor provisions or amendments thereto) commencing on the effective date of any registration statement relating to such underwritten public offering, unless the Company has granted its prior written consent to any such sale, short sale, loan, grant of option, pledge, other encumbrance or other disposition. The foregoing restrictions are intended and shall be construed so as to preclude any Participant from engaging in any hedging or other transaction that is designed to or reasonably could be expected to lead to or

result in, a sale or disposition of any shares of Common Stock during such period even if such shares of Common Stock are or would be disposed of by someone other than such Participant. Such prohibited hedging or other transactions would include, without limitation, any short sale (whether or not against the box) or any purchase, sale or grant of any right (including without limitation any put or call option) with respect to any shares of Common Stock or with respect to any security that includes, relates to, or derives any significant part of its value from any shares of Common Stock. Without limiting the generality and applicability of the foregoing provisions of this Section 9.5, if, in connection with any underwritten public offering of securities of the Company, the managing underwriter of such offering requires that the Company's then current directors and officers enter into a lock-up agreement, then (a) each Participant (regardless of whether or not such Participant has complied or complies with the provisions of clause (b) below) shall be bound by, and shall be deemed to have agreed to, the same lock-up terms as those to which the Company's directors and officers are required to adhere; and (b) at the request of the Company or such managing underwriter, each Participant shall execute and deliver a lock-up agreement in form and substance equivalent to that which is required to be executed by the Company's then current directors and officers.

9.6 Placement of Legends; Stop Orders; etc. Each share of Common Stock to be issued pursuant to Awards may bear a reference to the investment representations made in accordance with Section 9.3 in addition to any other applicable restrictions under the Plan, the terms of the Award and, if applicable, under any Stockholder Agreement or any other agreement between the Company and any Participant, and to the fact that no registration statement has been filed with the Securities and Exchange Commission in respect to such shares of Common Stock. All shares of Common Stock or other securities delivered under the Plan (as well as all certificates representing such shares of Common Stock or other securities) shall be subject to such

stop-transfer orders and other restrictions as the Committee may deem advisable under the rules, regulations, and other requirements of any stock exchange upon which the Common Stock is then listed, and any applicable federal or state securities law, and the Committee may cause a legend or legends to be placed on any such certificates to make appropriate reference to such restrictions.

9.7 Tax Withholding. Whenever shares of Common Stock are issued or to be issued pursuant to Awards, the Company shall have the right to require the recipient to remit to the Company an amount sufficient to satisfy federal, state, local or other withholding tax requirements if, when, and to the extent required by law (whether so required to secure for the Company an otherwise available tax deduction or otherwise) prior to the delivery of any certificate or certificates for such shares. The obligations of the Company under the Plan shall be conditional on satisfaction of all such withholding obligations and the Company shall, to the extent permitted by law, have the right to deduct any such taxes from any payment of any kind otherwise due to the recipient of an Award. However, in such cases Participants may elect, subject to the approval of the Committee, acting in its sole and absolute discretion, to satisfy an applicable withholding requirement, in whole or in part, by having the Company withhold shares to satisfy their tax obligations. Participants may only elect to have shares of Common Stock withheld having a Market Value on the date the tax is to be determined equal to the minimum statutory total tax which could be imposed on the transaction. All elections shall be irrevocable, made in writing, signed by the Participant, and shall be subject to any restrictions or limitations that the Committee deems appropriate

10. Reservation of Stock

The Company shall at all times during the term of the Plan and any outstanding Options granted hereunder reserve or otherwise keep available such number of shares of Common Stock as will be sufficient to satisfy the requirements of the Plan (if then in effect) and such Options and shall pay all fees and expenses necessarily incurred by the Company in connection therewith.

11. No Special Service Rights

Nothing contained in the Plan or in any Award Agreement shall confer upon any recipient of an Award any right with respect to the continuation of his or her employment, consulting, officer or Board member relationship or other association with the Company (or any Affiliate), or interfere in any way with the right of the Company (or any Affiliate), subject to the terms of any separate employment, consulting, officer or Board member agreement or provision of law or corporate articles or by-laws to the contrary, at any time to terminate such employment, consulting, officer or Board member agreement or to increase or decrease, or otherwise adjust, the other terms and conditions of the recipient's employment, consulting or Board member relationship or other association with the Company and its Affiliates.

12. Nonexclusivity of the Plan

Neither the adoption of the Plan by the Board nor the submission of the Plan to the stockholders of the Company shall be construed as creating any limitations on the power of the Board to adopt such other incentive arrangements as it may deem desirable, including without limitation, the granting of stock options, restricted stock and stock grants other than under the Plan, and such arrangements may be either applicable generally or only in specific cases.

13. Termination and Amendment of the Plan

The Board may at any time terminate the Plan or make such amendments or modifications of the Plan as it shall deem advisable. In the event of the termination of the Plan, the terms of the Plan shall survive any such termination with respect to any Award that is outstanding on the date of such termination, unless the holder of such Award agrees in writing to terminate such Award or to terminate all or any of the provisions of the Plan that apply to such Award. Unless the Board otherwise expressly provides, any amendment or modification of the Plan shall affect the terms of any Award outstanding on the date of such amendment or modification as well as the terms of any Award made from and after the date of such amendment or modification; *provided, however,* that except to the extent otherwise provided in the last sentence of this paragraph, (i) no amendment or modification of the Plan shall apply to any Award that is outstanding on the date of such amendment or modification if such amendment or modification would reduce the number of shares subject to such Award, increase the purchase price applicable to shares subject to such Award or materially adversely affect the provisions applicable to such Award that relate to the vesting or exercisability of such Award or of the shares subject to such Award, (ii) no amendment or modification of the Plan shall apply to any Incentive Option that is outstanding on the date of such amendment or modification if such amendment or modification would result in such Incentive Option no longer being treated as an "incentive stock option" within the meaning of Section 422 of the Code and (iii) no amendment or modification of the Plan shall apply to any Award that is outstanding on the date of such amendment or modification unless such amendment or modification of the Plan shall also apply to all other Awards outstanding on the date of such amendment or modification (except for those Awards to whom such amendment or modification is not applicable by

virtue of the provisions of the foregoing clause (ii) hereof). In the event of any amendment or modification of the Plan that is described in clause (i), (ii) or (iii) of the foregoing proviso, such amendment or modification of the Plan shall apply to any Award outstanding on the date of such amendment or modification only if the recipient of such Award consents in writing thereto.

The Committee may amend or modify, prospectively or retroactively, the terms of any outstanding Award without amending or modifying the terms of the Plan itself, provided that as amended or modified such Award is consistent with the terms of the Plan as in effect at the time of the amendment or modification of such Award, but no such amendment or modification of such Award shall, without the written consent of the recipient of such Award, reduce the number of shares subject to such Award, increase the purchase price applicable to shares subject to such Award, adversely affect the provisions applicable to such Award that relate to the vesting or exercisability of such Award or of the shares subject to such Award, or otherwise materially adversely affect the terms of such Award (except for amendments or modifications to the terms of such Award or of the stock subject to such Award that are expressly permitted by the terms of the Plan or that result from any amendment or modification of the Plan in accordance with the provisions of the first paragraph of this Section 13 or that are permitted by the provisions set forth below in this Section 13), or, if such Award is an Incentive Option, result in such Incentive Option no longer being treated as an “incentive stock option” within the meaning of Section 422 of the Code. Notwithstanding any of the foregoing provisions of this paragraph to the contrary, the Committee is expressly authorized to amend any or all outstanding Options to effect a repricing thereof by lowering the purchase price applicable to the shares of Common Stock subject to such Option or Options without the approval of the stockholders of the Company or the holder or holders of such Option or Options, and, in connection with such repricing, to amend or modify any of the other terms of the Option or Options so repriced, including, without limitation, for purposes of reducing the number of shares subject to such Option or Options or for purposes

of adversely affecting the provisions applicable to such Option or Options that relate to the vesting or exercisability thereof, in each case without the approval of stockholders of the Company or the holder or holders of such Option or Options.

In addition, notwithstanding anything express or implied in any of the foregoing provisions of this Section 13 to the contrary, the Committee may amend or modify, prospectively or retroactively, the terms of any outstanding Award to the extent the Committee reasonably determines necessary or appropriate to conform such Award to the requirements of Section 409A of the Code (concerning non-qualified deferred compensation), if applicable.

14. Interpretation of the Plan

In the event of any conflict between the provisions of this Plan and the provisions of any applicable Award Agreement, the provisions of this Plan shall control, except if and to the extent that the conflicting provision in such Award Agreement was authorized and approved by the Committee at the time of the grant of the Award evidenced by such Award Agreement or is ratified by the Committee at any time subsequent to the grant of such Award, in which case the conflicting provision in such Award Agreement shall control. Without limiting the generality of the foregoing provisions of this Section 14, insofar as possible the provisions of the Plan and such Award Agreement shall be construed so as to give full force and effect to all such provisions. In the event of any conflict between the provisions of this Plan and the provisions of any applicable Stockholder Agreement or other agreement between the Company and the applicable Participant, the provisions of such Stockholder Agreement or other agreement shall control except as required to fulfill the intention that this Plan constitute an incentive stock option plan within the meaning of Section 422 of the Code, but insofar as possible the provisions of the Plan and any such Stockholder Agreement or other agreement shall be construed so as to give full force and effect to all such provisions.

15. Notices and Other Communications

Any notice, demand, request or other communication hereunder to any party shall be deemed to be sufficient if contained in a written instrument delivered in person or duly sent by first class mail or overnight courier, postage prepaid, or telecopied with a confirmation copy by first class mail or overnight courier, addressed or telecopied, as the case may be, (i) if to the recipient of an Award, at his or her residence address last filed with the Company and (ii) if to the Company, at its principal place of business, addressed to the attention of its Chief Executive Officer, or to such other address or telecopier number, as the case may be, as the addressee may have designated by notice to the addressor. All such notices, requests, demands and other communications shall be deemed to have been received: (i) in the case of personal delivery, on the date of such delivery; (ii) in the case of mailing, five (5) days after having been sent by first class mail, postage prepaid; (iii) in the case of overnight courier, one (1) business day after deposit with a nationally recognized overnight courier, freight prepaid, specifying next business day delivery; and (iv) in the case of facsimile transmission, when sent and confirmed by facsimile machine report, if sent by facsimile transmission during normal business hours of the recipient, and if not sent during normal business hours, then on the recipient's next business day.

16. Governing Law

The Plan and all Award Agreements and actions taken thereunder shall be governed, interpreted and enforced in accordance with the laws of the State of Delaware, without regard to the conflict of laws principles thereof.

17. Adoption of Plan

This 2015 Equity Incentive Plan was approved and adopted on August 3, 2015, by the Board of Directors and on August 3, 2015, by the Sole Stockholder.

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TO
2015 EQUITY INCENTIVE PLAN

**Provisions Applicable to Award Recipients
Resident in California**

Until such time as the Company's Stock has been effectively registered under the Securities Act and if required by any applicable law, the following additional terms shall apply to Awards, and Stock issued pursuant to such Awards, granted under the Plan to persons resident in California as of the date of grant of the Award (each such person, a "California Recipient"). Capitalized terms not defined in this Attachment shall have the respective meanings set forth in the Plan.

1. No Option or other right to acquire Stock pursuant to an Award issued to any California Recipient, that is otherwise transferable pursuant to the terms of the Plan, shall be transferable other than by gift or domestic relations order to an immediate family member as that term is defined under applicable California and Federal securities law or to a revocable trust (or by will or the laws of descent and distribution).

2. The following limitations shall apply to the early expiration of Options granted California Recipients on account of termination of employment (unless employment is terminated for cause as defined by applicable law):

(a) Subject to Section 2(b) below, in the event the employment or other association with the Company and its Affiliates of an Optionee who is a California Resident is terminated, whether voluntary or otherwise and including on account of an entity ceasing to be an Affiliate of the Company, such California Recipient shall have at least thirty (30) days after the date of such termination (but in no event later than the expiration of the term of such Option as set forth in the Award Agreement) to exercise such Option to the extent exercisable as of the date of such termination.

(b) In the event that the employment or association with the Company and its Affiliates of an Optionee who is a California Resident is terminated as a result of death or disability, such California Recipient shall have at least six (6) months after the date of such termination (but in no event later than the expiration of the term of such Option as set forth in the Award Agreement) to exercise such Option to the extent exercisable as of the date of such termination.

3. The Plan must be approved by a majority of the outstanding securities entitled to vote within twelve (12) months before or after the later of (i) the date the Plan is adopted by the Company and (ii) the date on which any Option or other Award is granted to a California Recipient.

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**ATTACHMENT B
TO
2015 EQUITY INCENTIVE PLAN**

**RHYTHM PHARMACEUTICALS, INC.
2015 EQUITY INCENTIVE PLAN**

STOCK OPTION AGREEMENT

THIS STOCK OPTION AGREEMENT, dated as of [] , 20] (this "Agreement"), is between Rhythm Pharmaceuticals, Inc., a corporation organized under the laws of the State of Delaware (the "Company"), and the individual identified in paragraph 1 below, currently residing at the address set out at the end of this Agreement (the "Optionee"). Capitalized terms used in this Agreement without definition shall have the respective meaning ascribed to such capitalized terms in the Plan (as defined below).

1. **Grant of Option.** Pursuant and subject to the Company's 2015 Equity Incentive Plan (as the same may be amended from time to time, the "Plan"), the Company grants to you, the Optionee identified in the table below, an option (the "Option") to purchase from the Company all or any part of a total of the number of shares identified in the table below (the "Optioned Shares") of the common stock, par value \$0.001 per share, in the Company (the "Stock"), at the exercise price per share set out in the table below.

Optionee

Number of Shares

Exercise Price Per Share

Grant Date

Expiration Date(1)

2. **Character of Option.** This Option [is/is not](2) intended to be treated as an "incentive stock option" within the meaning of Section 422 of the Internal Revenue Code of 1986, as amended.

(1) For ISOs, not later than the day immediately preceding the tenth anniversary of the Grant Date.

(2) Either "is" or "is not", as the Committee or the Board has determined. If the Committee or the Board has determined that the option is a nonqualified stock option instead of an incentive stock option then the words should be "is not".

3. Expiration of Option. This Option shall expire at 5:00 p.m. EST on the Expiration Date or, if earlier, the earliest of the dates specified in whichever of the following applies:

- a) If the termination of your employment or other association is on account of your death or disability, the first anniversary of the date your employment ends.
- b) If the termination of your employment or other association is due to any other reason, three (3) months after your employment or other association ends.

4. Exercise of Option.

a) You may exercise this Option, in full or in part and at any time prior to the date this Option expires, as to the number of Optioned Shares for which this Option shall have become exercisable (the “Vested Shares”) pursuant Section 4(b) below. However, during any period that this Option remains outstanding after the end of your association with the Company and its Affiliates in any and all capacities as an officer, director, employee and/or consultant of the Company and its Affiliates, you may exercise it only to the extent of any remaining Vested Shares determined as of the effective time of the end of such association. The procedure for exercising this Option is described in Section 7.1(f) of the Plan; provided that in no event shall a fraction of a share of Stock be purchasable or deliverable upon exercise.

b) [Option1] [Subject to the provisions of Section 4(a) above, this Option shall become exercisable for the Optioned Shares over a period of four years as follows: (1) this Option shall become exercisable for twenty five percent (25%) of the Optioned Shares on [](3) (the “First Vesting Date”); and (2) this Option shall become exercisable for the remaining Optioned Shares in a series of thirty-six (36) equal monthly installments (except the last installment which, if necessary, may be smaller), with the first of such monthly installments becoming exercisable on [](4) and an additional monthly installment becoming exercisable on the first day of each calendar month thereafter until this Option shall have become exercisable for all of the Optioned Shares.(5)]

OR

(3) Enter date that is the one (1) year anniversary of Grant Date or, if the Option is a new hire award and the resolutions of the Committee or the Board approving the grant or award so provide, enter the date that is the one (1) year anniversary of the start date of employment or other association with the Company.

(4) Enter date that is the first day of the calendar month immediately following the calendar month in which the First Vesting Date occurs.

(5) The default vesting schedule contemplated by this form of Stock Option Agreement is a four year vesting schedule with a one year cliff vesting for 25% of the Optioned Shares and the balance of the Optioned Shares vesting monthly thereafter until all of the Optioned Shares are fully vested. If the resolutions of the Board or the Committee approving a particular grant or award provide for a different vesting schedule, then the default vesting schedule contemplated by this form of Stock Option Agreement should be modified to match the actual vesting schedule approved by the Committee or the Board for the particular grant or award.

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[Option 2] [Subject to the provisions of Section 4(a) above, this Option shall become exercisable for the number of Optioned Shares identified in the table below, in full or in part, at any time on or after the applicable exercise date or dates identified in the table:]

c)

<u>Number of Shares in Each Installment</u>	<u>Initial Exercise Date for Shares in Installment</u>

5. Transfer of Option. You may not transfer this Option except by will or the laws of descent and distribution, and, during your lifetime, only you may exercise this Option.

6. Incorporation of Plan Terms. This Option is granted subject to all of the applicable terms and provisions of the Plan, including but not limited to the limitations on the Company’s obligation to deliver Optioned Shares upon exercise set forth in Section 9 therein.

7. Tax Consequences. The Company makes no representation or warranty as to the tax treatment to you of your receipt or exercise of this Option or upon your sale or other disposition of the Optioned Shares. You should rely on your own tax advisors for such advice.

8. Treatment as Wages or Compensation. No amounts paid or payable in connection with this Option shall constitute wages or compensation for purposes of any applicable law, if ever, prior to the date on which such amount has been earned, vested and become payable in accordance with the terms of this Agreement and the Plan. No such amount shall be treated as wages or compensation for purposes of any employee or other benefit plan of the Company and its Affiliates except to the extent and at the time provided in the respective employee or other benefit plan.

9. Acknowledgements. You acknowledge that you have reviewed and understand the Plan and this Agreement in their entirety, and have had an opportunity to obtain the advice of counsel prior to executing this Agreement. You hereby agree to accept as binding, conclusive and final all decisions or interpretations of the Committee upon any questions arising under the Plan or this Agreement.

10. Further Assurances. The parties agree to execute such further instruments and to take such action as may reasonably be necessary to carry out the intent of this Agreement.

[11. **Community Property.** Without prejudice to the actual rights of the spouses as between each other, for all purposes of this Agreement, you shall be treated as agent and attorney-in-fact for that interest held or claimed by your spouse with respect to this Option]

and any Optioned Shares and the parties hereto shall act in all matters as if the Optionee was the sole owner of this Option and (following exercise) any such Optioned Shares. This appointment is coupled with an interest and is irrevocable.](6)

12. **Miscellaneous.** This Agreement shall be construed and enforced in accordance with the laws of the State of Delaware, without regard to the conflict of laws principles thereof and shall be binding upon and inure to the benefit of any successor or assign of the Company and any executor, administrator, trustee, guardian, or other legal representative of you. Capitalized terms used but not defined herein shall have the meaning assigned under the Plan. This Agreement may be executed in one or more counterparts all of which together shall constitute but one instrument. In making proof of this Agreement it shall not be necessary to produce or account for more than one such counterpart.

(6) Consider for inclusion for grants to California residents (and residents of other states with community property rules).

[The remainder of this page is intentionally left blank. Signature page to follow.]

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date first above written.

RHYTHM PHARMACEUTICALS, INC.

[NAME OF OPTIONEE]

By: _____

Signature of Optionee

Title: _____

Optionee's Address:

[Signature Page to Rhythm Pharmaceuticals, Inc. Stock Option Agreement]

**RHYTHM PHARMACEUTICALS, INC.
2015 EQUITY INCENTIVE PLAN**

OPTION EXERCISE FORM

Rhythm Pharmaceuticals, Inc.
500 Boylston Street, 11th Floor
Boston, MA 02116

Attention: Controller

Dear Sir:

In accordance with, and subject to the terms and conditions of, the Rhythm Pharmaceuticals, Inc. 2015 Equity Incentive Plan, as amended and in effect to date, I hereby elect to exercise my option granted under the agreement dated [] to purchase [] [()] shares of the common stock, par value \$0.001 per share, in Rhythm Pharmaceuticals, Inc. (the "Company").

Enclosed herewith is payment to the Company in the amount of [] Dollars (\$[]) in full payment of the option price of \$0.50 per share, for said shares. *[To be revised as necessary for non-cash payment of exercise price.]*

Sincerely yours,

Name:

ADOPTION AGREEMENT

This Adoption Agreement ("Adoption Agreement") is executed on , 2017, by the undersigned (the "Holder") pursuant to the terms of that certain Right of First Refusal and Co-Sale Agreement dated as of August 3, 2015 (the "Agreement"), as amended by the First Amendment dated as of January 6, 2017, by and among Rhythm Pharmaceuticals, Inc. (the "Company") and the Investors and Key Holders party thereto, as such Agreement may be amended or

amended and restated hereafter. Capitalized terms used but not defined in this Adoption Agreement shall have the respective meanings ascribed to such terms in the Agreement. By the execution of this Adoption Agreement, the Holder agrees as follows.

1.1 Acknowledgement. Holder acknowledges that Holder is acquiring shares of the Company (the “**Shares**”) and is not, as of the date hereof, a party to the Agreement as a Key Holder.

1.2 Agreement. Holder hereby (a) agrees that the Shares, and any other securities required by the Agreement to be bound thereby, shall be bound by and subject to the terms of the Agreement and (b) adopts the Agreement with the same force and effect as if Holder were originally a party thereto as a Key Holder thereunder.

1.3 Notice. Any notice required or permitted by the Agreement shall be given to Holder at the address or facsimile number listed below Holder’s signature hereto.

HOLDER:

By: _____
Name: _____

Address: _____

Facsimile Number: _____

Number of Shares: _____

ACCEPTED AND AGREED:

RHYTHM PHARMACEUTICALS, INC.

By: _____
Name: Keith Gottesdiener
Title: Chief Executive Officer

ADOPTION AGREEMENT

This Adoption Agreement (“**Adoption Agreement**”) is executed on _____, 2017, by the undersigned (the “**Holder**”) pursuant to the terms of that certain Investors’ Rights Agreement dated as of August 3, 2015 (the “**Agreement**”), by and among the Company and certain holders of securities of the Company, as such Agreement may be amended or amended and restated hereafter. Capitalized terms used but not defined in this Adoption Agreement shall have the respective meanings ascribed to such terms in the Agreement. By the execution of this Adoption Agreement, the Holder agrees as follows.

1.1 Acknowledgement. Holder acknowledges that Holder is acquiring certain Registrable Securities of the Company, and desires to become an Investor party to the Agreement with respect to such Registrable Securities.

1.2 Agreement. Holder hereby (a) agrees that the Registrable Securities and any other securities of the Company required by the Agreement to be bound thereby, shall be bound by and subject to the terms of the Agreement and (b) adopts the Agreement with the same force and effect as if Holder were originally an Investor party thereto.

1.3 Notice. Any notice required or permitted by the Agreement shall be given to Holder at the address or facsimile number listed below Holder’s signature hereto.

IN WITNESS WHEREOF, the parties have executed this Adoption Agreement as of the date first above written.

HOLDER:

By: _____
Name: _____

Address: _____

Facsimile Number: _____

ACCEPTED AND AGREED:

RHYTHM PHARMACEUTICALS, INC.

By: _____

Name: Keith Gottesdiener
Title: Chief Executive Officer

ADOPTION AGREEMENT

This Adoption Agreement ("Adoption Agreement") is executed on , 2017, by the undersigned (the "Holder") pursuant to the terms of that certain Voting Agreement dated as of August 3, 2015 (the "Agreement"), by and among the Company and certain holders of securities of the Company, as such Agreement may be amended or amended and restated hereafter. Capitalized terms used but not defined in this Adoption Agreement shall have the respective meanings ascribed to such terms in the Agreement. By the execution of this Adoption Agreement, the Holder agrees as follows.

1.1 Acknowledgement. Holder acknowledges that Holder is acquiring certain Shares for one of the following reasons (Check the correct box):

- As a transferee of Shares from a party in such party's capacity as an "Investor" bound by the Agreement, and after such transfer, Holder shall be considered an "Investor" and a "Stockholder" for all purposes of the Agreement with respect to such Shares. Notwithstanding the foregoing, a transferee of shares of Common Stock from Rhythm Holding Company, LLC that meets the criteria set forth in Subsection 8.2 of the Agreement requiring such transferee to become an "Key Holder" under the Agreement should not check this box but should check the box immediately below.
- As a transferee of shares of Common Stock from Rhythm Holding Company, LLC if such transferee meets the criteria set forth in Subsection 8.2 of the Agreement requiring such transferee to become a "Key Holder" under the Agreement, and after such transfer, Holder shall be considered a "Key Holder" and a "Stockholder" for all purposes of the Agreement with respect to such Shares.
- As a transferee of Shares from a party in such party's capacity as a "Key Holder" bound by the Agreement, and after such transfer, Holder shall be considered a "Key Holder" and a "Stockholder" for all purposes of the Agreement with respect to such Shares.
- As a new Investor in accordance with Subsection 8.1(a) of the Agreement, in which case Holder will be an "Investor" and a "Stockholder" for all purposes of the Agreement with respect to the Shares acquired by such new Investor as contemplated under Subsection 8.1(a) of the Agreement.
- In accordance with Subsection 8.1(b) of the Agreement, as a new party who is not a new Investor, in which case Holder will be a "Key Holder" and "Stockholder" for all purposes of the Agreement with respect to the Shares acquired by such new party as contemplated under Subsection 8.1(b) of the Agreement.

1.2 Agreement. Holder hereby (a) agrees that the Shares and any other securities of the Company required by the Agreement to be bound thereby, shall be bound by and subject to the terms of the Agreement and (b) adopts the Agreement with the same force and effect as if Holder were originally a party thereto.

1.3 Notice. Any notice required or permitted by the Agreement shall be given to Holder at the address or facsimile number listed below Holder's signature hereto.

[Signature Page to Follow]

IN WITNESS WHEREOF, the parties have executed this Adoption Agreement as of the date first above written.

HOLDER:

By: _____
Name: _____

Address:

Facsimile Number:

ACCEPTED AND AGREED:

RHYTHM PHARMACEUTICALS, INC.

By: _____

Name: Keith Gottesdiener
Title: Chief Executive Officer

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption "Experts" and to the use of our report dated May 23, 2017, except for Note 13, as to which the date is September 22, 2017 in Amendment No.1 to the Registration Statement (Form S-1) and related Prospectus of Rhythm Pharmaceuticals, Inc. for the registration of 7,666,666 shares of its common stock.

/s/ Ernst & Young LLP

Boston, Massachusetts
September 22, 2017

QuickLinks

[Exhibit 23.1](#)