
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

FORM 10-Q

QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the quarterly period ended September 30, 2018
OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from _____ to _____
Commission file number 001-38223

RHYTHM PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

46-2159271
(I.R.S. Employer
Identification No.)

500 Boylston Street
11th Floor
Boston, MA 02116
(Address of principal executive offices)
(Zip Code)

(857) 264-4280
(Registrant's telephone number, including area code)

Unchanged
(Former name, former address and former fiscal year, if changed since last report)

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15 (d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No
Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes No
Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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.

Large accelerated filer

Accelerated filer

Non-accelerated filer

Smaller reporting company

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.

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes No .

The number of shares outstanding of the registrant's Common Stock as of November 8, 2018 was 34,410,725.

RHYTHM PHARMACEUTICALS, INC.

FORM 10-Q

INDEX

	<u>Page No.</u>
<u>PART I FINANCIAL INFORMATION</u>	
<u>Item 1. Condensed Consolidated Financial Statements (Unaudited)</u>	3
<u>Condensed Consolidated Balance Sheets</u>	3
<u>Condensed Consolidated Statements of Operations and Comprehensive Loss</u>	4
<u>Condensed Consolidated Statements of Cash Flows</u>	5
<u>Notes to Unaudited Condensed Consolidated Financial Statements</u>	6
<u>Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations</u>	16
<u>Item 3. Quantitative and Qualitative Disclosures About Market Risk</u>	27
<u>Item 4. Controls and Procedures</u>	28
<u>PART II OTHER INFORMATION</u>	28
<u>Item 1. Legal Proceedings</u>	28
<u>Item 1A. Risk Factors</u>	29
<u>Item 2. Unregistered Sales of Equity Securities and Use of Proceeds</u>	79
<u>Item 3. Defaults Upon Senior Securities</u>	80
<u>Item 4. Mine Safety Disclosure</u>	80
<u>Item 5. Other Information</u>	80
<u>Item 6. Exhibits</u>	81
<u>SIGNATURES</u>	82

PART I – FINANCIAL INFORMATION**Item 1. Financial Statements.**

Rhythm Pharmaceuticals, Inc.
Condensed Consolidated Balance Sheets
(in thousands, except share and per share data)

	(Unaudited) September 30, 2018	December 31, 2017
Assets		
Current assets:		
Cash and cash equivalents	\$ 58,247	\$ 34,236
Short-term investments	214,139	113,846
Prepaid expenses and other current assets	4,152	2,589
Total current assets	276,538	150,671
Property, plant and equipment, net	939	840
Restricted cash	251	225
Total assets	<u>\$ 277,728</u>	<u>\$ 151,736</u>
Liabilities, convertible preferred stock and stockholders' equity		
Current liabilities:		
Accounts payable	\$ 208	\$ 2,427
Deferred rent	—	83
Accrued expenses and other current liabilities	7,595	4,210
Total current liabilities	7,803	6,720
Long-term liabilities:		
Deferred rent	288	228
Total liabilities	8,091	6,948
Commitments and contingencies		
Preferred stock:		
Convertible Preferred Stock, \$0.001 par value: 10,000,000 shares authorized; no shares issued and outstanding at September 30, 2018 and December 31, 2017, respectively	—	—
Stockholders' equity:		
Common stock, \$0.001 par value: 120,000,000 shares authorized; 34,382,525 and 27,284,140 shares issued and outstanding September 30, 2018 and December 31, 2017, respectively	34	27
Additional paid-in capital	428,698	255,013
Accumulated deficit	(159,095)	(110,252)
Total stockholders' equity	269,637	144,788
Total liabilities, convertible preferred stock and stockholders' equity	<u>\$ 277,728</u>	<u>\$ 151,736</u>

The accompanying notes are an integral part of these financial statements

Rhythm Pharmaceuticals, Inc.
Condensed Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)
(Unaudited)

	<u>Three months ended September 30,</u>		<u>Nine months ended September 30,</u>	
	<u>2018</u>	<u>2017</u>	<u>2018</u>	<u>2017</u>
Operating expenses:				
Research and development	\$ 10,705	\$ 5,971	\$ 31,575	\$ 16,241
Selling, general, and administrative	8,539	2,315	19,691	5,188
Total operating expenses	19,244	8,286	51,266	21,429
Loss from operations	(19,244)	(8,286)	(51,266)	(21,429)
Other income (expense):				
Revaluation of Series A Investor Instrument and Series A Investor Right/Obligation	—	(1,781)	—	(1,863)
Interest income, net	1,558	51	2,709	114
Total other income (expense):	1,558	(1,730)	2,709	(1,749)
Net loss and comprehensive loss	\$ (17,686)	\$ (10,016)	\$ (48,557)	\$ (23,178)
Net loss attributable to common stockholders	\$ (17,686)	\$ (11,429)	\$ (48,557)	\$ (26,963)
Net loss attributable to common stockholders per common share, basic and diluted	\$ (0.52)	\$ (1.78)	\$ (1.63)	\$ (3.02)
Weighted average common shares outstanding, basic and diluted	34,256,519	6,404,254	29,859,314	8,918,389

The accompanying notes are an integral part of these financial statements

Rhythm Pharmaceuticals, Inc.
Condensed Consolidated Statements of Cash Flows
(in thousands, except share and per share data)
(Unaudited)

	Nine months ended September 30,	
	2018	2017
Operating activities		
Net loss	\$ (48,557)	\$ (23,178)
Adjustments to reconcile net loss to cash used in operating activities:		
Non-cash research and development license expense	4,448	—
Stock-based compensation expense	4,367	1,569
Depreciation and amortization	228	163
Non-cash rent expense	(23)	(56)
Mark to market revaluation of series A investor instrument	—	1,863
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(2,760)	(972)
Deferred issuance costs	—	(1,689)
Accounts payable, accrued expenses and other current liabilities	1,224	830
Due to related parties	—	(105)
Net cash used in operating activities	<u>(41,073)</u>	<u>(21,575)</u>
Investing activities		
Purchases of short-term investments	(188,559)	(13,021)
Maturities of short-term investments	89,463	14,506
Purchases of property, plant and equipment	(327)	(78)
Net cash provided by (used in) investing activities	<u>(99,423)</u>	<u>1,407</u>
Financing activities		
Net proceeds from issuance of common stock	162,899	—
Proceeds from the exercise of stock options	1,634	700
Net proceeds from issuance of Series A Convertible Preferred Stock	—	40,842
Net cash provided by financing activities	<u>164,533</u>	<u>41,542</u>
Net increase in cash, cash equivalents and restricted cash	24,037	21,374
Cash, cash equivalents and restricted cash at beginning of period	34,461	6,765
Cash, cash equivalents and restricted cash at end of period	<u>\$ 58,498</u>	<u>\$ 28,139</u>

The accompanying notes are an integral part of these financial statements

Rhythm Pharmaceuticals, Inc.

Notes to Unaudited Condensed Consolidated Financial Statements

(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 therapeutics for the treatment of rare genetic disorders that result in severe, 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 peptide for the treatment of rare genetic disorders of obesity caused by 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. The Company is currently evaluating setmelanotide for the treatment of 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. The Company believes 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.

In March 2018 the Company acquired exclusive, worldwide rights from Takeda Pharmaceutical Company Limited (“Takeda”) to develop and commercialize T-3525770 (now “RM-853”). RM-853 is a potent, orally available ghrelin o-acetyltransferase (“GOAT”) inhibitor currently in preclinical development for Prader-Willi Syndrome (“PWS”). PWS is a rare genetic disorder that results in hyperphagia and early-onset, life-threatening obesity, for which there are no approved therapeutic options.

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 5 for further discussion).

Liquidity

The Company has incurred operating losses and negative cash flows from operations since inception. As of September 30, 2018, the Company had an accumulated deficit of \$159,095. The Company has primarily funded these

losses through capital contributions received from the LLC entity and the sale of preferred and common stock to outside investors. To date, the Company has no product revenue and 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 September 30, 2018, the Company had \$272,386 of cash and cash equivalents and short-term investments on hand. In the future, the Company will be dependent on obtaining funding from third parties, such as proceeds from the issuance of debt, sale of equity, and funded research and development programs, to maintain the Company's operations and meet the Company's obligations. There is no guarantee that additional equity or other financings will be available to the Company on acceptable terms, or at all. If the Company fails to obtain additional funding when needed, the Company would be forced to scale back, terminate its operations or seek to merge with or be acquired by another company. Management believes that the Company's existing cash resources will be sufficient to fund the Company's operating plan into the second half of 2020.

2. Summary of Significant Accounting Policies

Basis of Presentation

The Company's unaudited condensed consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States ("GAAP") and the applicable rules and regulations of the Securities and Exchange Commission ("SEC") regarding interim financial reporting. 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"). As permitted under these rules, certain footnotes or other financial information that are normally required by GAAP have been condensed or omitted.

The accompanying interim balance sheet as of September 30, 2018, the statements of operations and comprehensive loss for the three and nine months ended September 30, 2018 and 2017, the statement of cash flows for the nine months ended September 30, 2018 and 2017 and the related footnote disclosures are unaudited. 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 all normal recurring adjustments necessary for the fair presentation of the interim financial statements. The results for the nine months ended September 30, 2018 are not necessarily indicative of the results expected for the full fiscal year.

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.

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 have been retrospectively adjusted for all periods presented to give effect of the reverse stock split.

On October 5, 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 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.

On October 10, 2017 the Company completed its initial public offering ("IPO") of 8,107,500 shares of common stock at an offering price of \$17.00 per share, which included the exercise in full by the underwriters of their option to purchase up to 1,057,500 additional shares of common stock. The Company received gross proceeds of approximately \$137,828 or net proceeds of \$125,658 after deducting underwriting discounts, commissions and estimated offering expenses. In connection with the IPO, the Company's outstanding shares of convertible preferred stock were automatically converted into 17,406,338 shares of common stock.

[Table of Contents](#)

On June 25, 2018 the Company completed its public offering of 6,591,800 shares of common stock at an offering price of \$26.42 per share, which included the exercise in full by the underwriters of their option to purchase up to 859,800 additional shares of common stock. The Company received gross proceeds of approximately \$174,155 or net proceeds of \$162,899 after deducting underwriting discounts, commissions and offering expenses.

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 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 Instrument (see Note 4).

Principles of Consolidation

The consolidated financial statements include the accounts of Rhythm Pharmaceuticals, Inc. and its subsidiaries. All significant intercompany balances and transactions have been eliminated in consolidation.

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.

2017 Series A Investor Instrument

The Company has classified its 2017 Series A Investor Instrument (See Note 4) as a liability as it is a free-standing financial instrument. The 2017 Series A Investor Instrument was recorded at fair value upon the issuance of the Company's series A preferred stock in January 2017, and subsequently remeasured to fair value at each reporting period. Changes in fair value of the financial instrument is recognized as a component of other income (expense), net in the statement of operations and comprehensive loss. 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 Company used the Black-Scholes option-pricing model, which incorporates assumptions and estimates, to value the 2017 Series A Investor Call Option 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 Option, 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

[Table of Contents](#)

consideration the most recent sale of our convertible preferred stock and the investors' right to invest in a subsequent tranche. As the Company was a private company and lacked company-specific historical and implied volatility information of its stock, it estimated 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 Option. 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 Option. 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.

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 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.

The following table includes the potential common shares, presented based on amounts outstanding at each period end, that were excluded from the computation of diluted net loss per share attributable to common stockholders for the periods indicated:

	September 30,	
	2018	2017
Stock options	2,474,790	1,821,579
Series A convertible preferred shares	—	8,827,698
Total	2,474,790	10,649,277

Basic and diluted earnings per share is calculated as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Numerator:				
Net loss	\$ (17,686)	\$ (10,016)	\$ (48,557)	\$ (23,178)
Cumulative dividends on convertible preferred shares	—	(1,413)	—	(3,785)
Loss attributable to common shares—basic and diluted	<u>\$ (17,686)</u>	<u>\$ (11,429)</u>	<u>\$ (48,557)</u>	<u>\$ (26,963)</u>
Denominator:				
Weighted-average number of common shares—basic and diluted	34,256,519	6,404,254	29,859,314	8,918,389
Loss per common share—basic and diluted	<u>\$ (0.52)</u>	<u>\$ (1.78)</u>	<u>\$ (1.63)</u>	<u>\$ (3.02)</u>

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 matters that require additional disclosure. Subsequent events have been evaluated as required.

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.

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 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 adopted ASU on January 1, 2018 and has applied its content to the statement of cash flows for the nine months ended September 30, 2018 and 2017 presented herein.

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 did not have a material impact on the Company's financial position or results of operations.

In June 2018, the FASB issued ASU 2018-07, Compensation-Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting, (“ASU 2018-07”). ASU 2018-07 expands the scope of Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees. An entity should apply the requirements of Topic 718 to nonemployee awards except for certain exemptions specified in the amendment. This ASU is effective for fiscal years, and interim periods within those years, beginning after December 15, 2018, and early adoption is permitted. The Company has early adopted ASU 2018-07 in July 2018. The guidance has been adopted using the modified-retrospective approach, which requires that unsettled equity-classified awards for which a measurement date has not been established to be measured using the adoption date fair value. The adoption of this ASU did not have a material impact on the Company's financial position or results of operations.

3. Accrued Expenses

Accrued expenses consisted of the following:

	September 30, 2018	December 31, 2017
Research and development costs	\$ 4,909	\$ 2,771
Professional fees	1,286	327
Payroll related	1,355	1,094
Other	45	18
Accrued expenses	<u>\$ 7,595</u>	<u>\$ 4,210</u>

4. Fair Value of Financial Assets and Liability

As of September 30, 2018 and December 31, 2017, the carrying amount of cash and cash equivalents and short-term investments was \$272,386 and \$148,082, 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 \$57,856 and \$34,698 as of September 30, 2018 and December 31, 2017, respectively. The financial assets valued based on level 2 inputs consist of corporate debt securities and commercial paper, which consist of investments in highly-rated investment-grade corporations.

A financial liability was recognized by the Company during the nine months ended September 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. Upon the closing of the second tranche of the 2017 Series A preferred financing in August 2017, this liability was settled.

The following tables present information about the Company's financial assets 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 September 30, 2018 using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash Equivalents:				
Corporate Debt Securities and Commercial Paper	\$ —	\$ —	\$ —	\$ —
Money Market Funds	57,856	—	—	57,856
Marketable Securities:				
Corporate Debt Securities and Commercial Paper	—	214,139	—	214,139
U.S. Treasury Securities	—	—	—	—
Total	<u>\$ 57,856</u>	<u>\$ 214,139</u>	<u>\$ —</u>	<u>\$ 271,995</u>

[Table of Contents](#)

	Fair value Measurements as of December 31, 2017 using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash Equivalents:				
Corporate Debt Securities	\$ —	\$ 15,104	\$ —	\$ 15,104
Money Market Funds	17,753	—	—	17,753
Marketable Securities:				
Corporate Debt Securities	—	96,901	—	96,901
U.S. Treasury Securities	16,945	—	—	16,945
Total	\$ 34,698	\$ 112,005	\$ —	\$ 146,703

Marketable Securities

The following tables summarize the Company's marketable securities:

	September 30, 2018			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Assets				
Corporate Debt Securities and Commercial Paper (due within 1 year)	\$ 214,225	\$ 4	\$ (90)	\$ 214,139
U.S. Treasury Securities (due within 1 year)	—	—	—	—
	\$ 214,225	\$ 4	\$ (90)	\$ 214,139

	December 31, 2017			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Assets				
Corporate Debt Securities (due within 1 year)	\$ 97,029	\$ —	\$ (128)	\$ 96,901
U.S. Treasury Securities (due within 1 year)	16,958	—	(13)	16,945
	\$ 113,987	\$ —	\$ (141)	\$ 113,846

Below is a roll forward of the fair value of the 2017 Series A Investor Instrument for the nine months ended September 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	1,863
Reclassification of liability upon August 2017 Second Tranche Closing	(2,191)
Fair value at September 30, 2017	\$ —

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.

[Table of Contents](#)

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:

	August 2017 Second Tranche Closing
Series A Convertible Preferred Stock Exercise Price	\$ 1.00
Series A Convertible Preferred Stock Fair Value	\$ 1.33
Expected term	1.5 months
Expected volatility	64.0 %
Expected interest rate	0.95 %
Expected dividend yield	—

In August 2017, upon the closing of the second tranche of the series A preferred stock financing, the 2017 Series A Investor Call Option expired unexercised.

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 October 15, 2017 and a nominal, risk-free discount rate.

5. Preferred and Common Stock

Preferred Stock

Upon the closing of the IPO, the series A convertible preferred stock automatically converted into shares of common stock on a 9.17-for-1 basis.

Common Stock

In March 2013, the Company issued 10,196,292 shares of common stock at a purchase price of \$0.001 per share. Prior to August, 2017, the LLC entity owned all of these shares.

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 converted to common stock on a 9.17-to-1 basis upon the closing of the IPO in October 2017.

In September 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 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.

On October 10, 2017 the Company completed its IPO of 8,107,500 shares of common stock at an offering price of \$17.00 per share, which included the exercise in full by the underwriters of their option to purchase up to 1,057,500 additional shares of common stock. The Company received gross proceeds of approximately \$137,828 or net proceeds of \$125,658 after deducting underwriting discounts, commissions and estimated offering expenses. In connection with the IPO, the Company's outstanding shares of convertible preferred stock were automatically converted into 17,406,338 shares of common stock.

On April 3, 2018, in association with the Takeda license agreement, the Company issued 223,544 shares of common stock. See Note 6 for further discussion.

On June 25, 2018 the Company completed its public offering of 6,591,800 shares of common stock at an offering price of \$26.42 per share, which included the exercise in full by the underwriters of their option to purchase up to 859,800 additional shares of common stock. The Company received gross proceeds of approximately \$174,155 or net proceeds of \$162,899 after deducting underwriting discounts, commissions and offering expenses.

6. 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 3 clinical trials, and relamorelin. 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 July 2017, the Company made a prepayment on the first milestone event associated with this license agreement. The first milestone relates to the initiation of a Phase 3 study for setmelanotide in a pivotal multi-center human clinical trial in a large number of patients. The prepayment associated with this milestone was \$1,000 and was recorded as research and development expenses during the three months ended March 31, 2018 when the milestone criteria was met in full.

In January 2016, the Company entered into a license 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, mid to mid-high single digit royalties, 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 that 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.

In December 2017, the Company achieved the second milestone event associated with this license agreement. The Company completed the Phase I proof of concept study using the Camurus drug delivery technology. The fee associated with this second milestone was \$1,000 and was recorded as research and development expense.

In March 2018, the Company entered into a license agreement with Takeda, for the rights of a program that includes the clinical candidate RM-853, which is a GOAT inhibitor, which is currently in preclinical development for PWS. Pursuant to the license agreement the Company was required to pay a non-refundable and non-creditable signing fee, which the Company settled by issuing on April 3, 2018, 223,544 shares of common stock valued at \$4,448. Under the terms of the license agreement, assuming that RM-853 is successfully developed, receives regulatory approval and is commercialized, the Company is also required to pay up to \$70,000 in one-time, non-refundable development milestone payments upon the achievement of certain clinical and regulatory milestones. The Company is also required to pay up to \$70,000 in one-time, non-refundable, non-creditable sales milestone payments upon the achievement of certain sales levels. The Company is also required to pay to Takeda, mid to mid-high single digit royalties (subject to certain potential

reductions over time), on a product-by-product and country-by-country basis of annual net sales, of each product in such country, beginning on the first commercial sale of a product in such country, and continuing until the latest 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 a Takeda patents covering the composition or use of such product in such country; or (iii) the expiration of all regulatory exclusivity for such product in such country. The Company recorded the fair value of the common stock to be issued to the licensors as research and development expense, as the license does not have a future alternative use, in accordance with ASC Topic 730, *Research and Development*.

7. Related-Party Transactions

Expenses paid directly to consultants and vendors considered to be related parties amounted to \$542, \$1,294, \$1,518 and \$1,880 for the three and nine months ended September 30, 2018 and 2017, respectively. Outstanding payments due to these related parties as of September 30, 2018 and December 31, 2017 were \$156 and \$112, respectively, and were included within accounts payable on the balance sheet.

8. Income Taxes

For the year ended December 31, 2017, 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.

Item 2. 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 unaudited condensed consolidated financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions, including statements regarding our financial performance, including our expectations regarding our existing cash, operating losses, expenses and sources of future financing; statements regarding our ability to hire and retain necessary personnel; statements regarding patient enrollments and the timing thereof; statements regarding the timing of announcements regarding results of clinical trials; statements regarding our ability to protect our intellectual property; statements regarding our ability to negotiate our collaboration agreements, if needed; statements regarding our marketing, commercial sales, and revenue generation; and other statements identified by words such as "anticipates," "believes," "could," "estimates," "expects," "intends," "may," "might," "likely," "plans," "potential," "predicts," "projects," "seeks," "should," "target," "will," "would," or similar expressions and the negatives of those terms include forward looking statements that involve risks and uncertainties. Forward-looking statements are not promises or guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, and which could cause actual results to differ materially from those contemplated in such forward-looking statements. These factors include those set forth in Part II, Item 1A under the heading "Risk Factors" of this Quarterly Report on Form 10-Q. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors. We discuss factors that we believe could cause or contribute to these differences below and elsewhere in this report, including those set forth in Part II, Item 1A under the heading "Risk Factors" of this Quarterly Report on Form 10-Q.

Overview

We are a biopharmaceutical company focused on the development and commercialization of therapeutics for the treatment of rare genetic disorders that result in severe, 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, Bardet-Biedl syndrome and Alström syndrome, four 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 the 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 pathways. The Breakthrough Therapy designation currently covers indications for: POMC deficiency obesity, LepR deficiency obesity, Bardet-Biedl syndrome and Alström Syndrome. Setmelanotide is currently in Phase 3 development for POMC deficiency obesity and LepR deficiency obesity, and we are initiating a combined Phase 3 trial for Bardet-Biedl and Alström syndrome. We have completed enrollment in the pivotal cohorts for both our POMC deficiency obesity Phase 3 clinical trial and our LepR deficiency obesity Phase 3 clinical trial. We expect to report initial Phase 3 data from these trials in the third quarter of 2019, and subsequently plan to file for regulatory approval for these two indications concurrently. We believe that we have demonstrated proof of concept in our Phase 2 clinical trial in Bardet-Biedl syndrome and Alström syndrome, and met with the FDA in May 2018 to discuss a combined pivotal Phase 3 clinical trial in these indications. Based on these preliminary discussions with the FDA, we currently plan to initiate this trial and enroll patients in 2018. We have an ongoing Phase 2 clinical trial in POMC heterozygous deficiency obesity and POMC epigenetic disorders. We reported initial, preliminary results in these additional Phase 2 indications in June 2018, and plan to provide a further update for these indications early in 2019. In total, approximately 300 obese subjects and patients

[Table of Contents](#)

have been treated with setmelanotide in previous and ongoing clinical trials in which setmelanotide demonstrated statistically significant weight loss with good tolerability.

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 forty-three employees. Of these employees, twenty-eight are engaged in research and development activities, six are engaged in pre-commercialization activities and nine are engaged in support administration, including business development and finance. In the near-term, we expect to significantly expand our clinical, commercial and finance personnel, in particular, and will incur increased expenses as a result.

In March 2018 we acquired exclusive, worldwide rights from Takeda Pharmaceutical Company Limited, or Takeda, to develop and commercialize T-3525770 (now “RM-853”). RM-853 is a potent, orally available ghrelin o-acyltransferase, or GOAT, inhibitor currently in preclinical development for Prader-Willi Syndrome, or PWS. PWS is a rare genetic disorder that results in hyperphagia and early-onset, life-threatening obesity, for which there are no approved therapeutic options. We will assume sole responsibility for the global product development and commercialization of RM-853. Takeda received an upfront fee of \$4.4 million which we settled in April 2018 with shares of our common stock, and will receive back-end development milestones, and single-digit royalties on future RM-853 sales.

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 the private placement of equity securities to outside investors. On October 10, 2017 we completed our initial public offering, or IPO, of 8,107,500 shares of common stock at an offering price of \$17.00 per share, which included the exercise in full by the underwriters of their option to purchase up to 1,057,500 additional shares of common stock. We received gross proceeds of approximately \$137.8 million, before deducting underwriting discounts, commissions and offering related transaction costs. In connection with the IPO, our outstanding shares of convertible preferred stock were automatically converted into 17,406,338 shares of common stock. On June 25, 2018 we completed our public offering of 6,591,800 shares of common stock at an offering price of \$26.42 per share, which included the exercise in full by the underwriters of their option to purchase up to 859,800 additional shares of common stock. We received gross proceeds of approximately \$174.2 million before deducting underwriting discounts, commissions and offering expenses. 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 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.

As of September 30, 2018, we had an accumulated deficit of \$159.1 million. Our net losses were \$17.7 million, \$10.0 million, \$48.6 million and \$23.2 million for the three and nine months ended September 30, 2018 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 contract manufacturing organizations, or 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 September 30, 2018, our existing cash and cash equivalents and short-term investments were approximately \$272.4 million. We expect that our existing cash and cash equivalents and short-term investments will enable us to fund our operating expenses into the second half of 2020.

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 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 Investigational New Drug Application, or 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 January 2017 and August 2017, we sold 20,475,001 shares and 20,474,998 shares, respectively, of our series A convertible preferred stock to certain investors. Following the closing of our series A convertible 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 converted into shares of our common stock on a 9.17-for-1 basis upon the closing of our IPO. Following the Distribution, the LLC entity did not own any of our common stock.

In connection with our IPO, we effected a 1-for-9.17 reverse stock split of our outstanding common stock on September 29, 2017. All share and per share amounts in the financial statements have been retrospectively adjusted for all periods presented to give effect of the reverse stock split.

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 expenses:

Research and development summary	Three Months Ended		Nine Months Ended	
	September 30,		September 30,	
	2018	2017	2018	2017
Research and development expense	<u>\$10,705</u>	<u>\$5,971</u>	<u>\$31,575</u>	<u>\$16,241</u>

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.

Selling, general and administrative expenses

Selling expenses consist of professional fees related to preparation for the eventual commercialization of setmelanotide, if approved, as well as salaries and related benefits for commercial employees, including stock-based compensation. As we accelerate our preparation for commercialization and, if it is approved, start to market setmelanotide and as we explore new collaborations to develop and commercialize setmelanotide, we anticipate that these expenses will materially increase.

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, relating to our full-time employees. Other significant costs include rent, legal fees relating to patent and corporate matters and fees for accounting and consulting services.

The following table summarizes our current selling, general and administrative expenses:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Selling, general and administrative summary				
Selling, general and administrative expense	\$ 8,539	\$ 2,315	\$ 19,691	\$ 5,188

We anticipate that our selling, 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 Quarterly Report on Form 10-Q, 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.

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.

2017 Series A Investor Instrument

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 at a purchase price of \$1.00 per share in January 2017. The series A preferred 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 2017 Series A Investor Instrument (See Note 4 to our financial statements included elsewhere in this Quarterly Report on Form 10-Q) as a liability as it is a free-standing financial instrument. The 2017 Series A Investor Instrument was recorded at fair value upon the issuance of our series A preferred stock in January 2017, and subsequently remeasured to fair value at each reporting period. Changes in fair value of this financial instrument is recognized as a component of other income (expense), net in the statement of operations and comprehensive loss. We estimated the fair value of the 2017 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 2017 Series A Investor Call Option 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 2017 Series A Investor Call Option, 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 were a private company and lacked 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 2017 Series A Investor Call Option. 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 2017 Series A Investor Call

Option. 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.

Stock-based compensation

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 our IPO, or the 2015 Plan, which we terminated upon consummation of our IPO and replaced with the 2017 equity incentive plan, or the 2017 Plan. The 2017 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 5,109,904 shares of common stock under the 2017 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 2017 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 2017 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. Previously 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 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. Upon adopting ASU 2016-09, *Improvements to Employee Share-Based Payment Accounting (Topic 718)* on January 1, 2017, we have elected to account for forfeitures as they occur.

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 upon the technical merits of the tax position as well as consideration of the available facts and circumstances. As of December 31, 2017, 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.

As of December 31, 2017, we had net operating loss carryforwards to reduce federal and state incomes taxes of approximately \$73.1 million and \$3.8 million, respectively. If not utilized, these carryforwards begin to expire in 2033. At December 31, 2017, we also had available research and development tax credits for federal and state income tax purposes of approximately \$1.9 million and \$0.5 million, respectively. The federal and state credits begin to expire in 2033 and 2028, respectively. Additionally, as of December 31, 2017, we had a federal orphan drug credits related to qualifying research of \$2.3 million. These tax credit carryforwards begin to expire in 2033 for federal purposes and 2028 for state purposes.

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 Internal Revenue Code of 1986, as amended, or 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.

Results of Operations

Comparison of the three months ended September 30, 2018 and 2017

The following table summarizes our results of operations for the three months ended September 30, 2018 and 2017, together with the changes in those items in dollars and as a percentage:

	Three Months Ended		Change	
	2018	2017	\$	%
	(in thousands)			
Statement of Operations Data:				
Operating Expenses:				
Research and development	\$ 10,705	\$ 5,971	\$ 4,734	79 %
Selling, general, and administrative	8,539	2,315	6,224	269 %
Total operating expenses	19,244	8,286	10,958	132 %
Loss from operations	(19,244)	(8,286)	(10,958)	132 %
Other (expense) income, net	1,558	(1,730)	3,288	NM %
Net loss and comprehensive loss	\$ (17,686)	\$ (10,016)	\$ (7,670)	77 %

Research and development expense. Research and development expense increased by \$4.7 million to \$10.7 million in 2018 from \$6.0 million in 2017, an increase of 79%. The increase was primarily due to \$1.3 million in employee related costs due to the hiring of additional personnel during the second half of 2017 and throughout 2018, an increase of \$1.2 million related to genetic sequencing efforts designed to improve identification of patients with MC4 pathway deficiencies as well as supplemental work related to our future new drug application (“NDA”) for setmelanotide, a \$0.9 million increase related to an increase in patient visits and the number of investigator sites for new and existing clinical trials and a \$0.6 million increase in travel and sponsorship related expenses for conferences attended during the three months ended September 30, 2018.

Selling, general and administrative expense. Selling, general and administrative expense increased by \$6.2 million to \$8.5 million in 2018 from \$2.3 million in 2017, an increase of 269%. The increase was primarily due to a \$1.4 million increase of employee related costs attributable to hiring additional personnel to support our growing organization, and an increase of \$4.0 million for the development and building of our commercial organization to drive patient identification and consulting services supporting our disease awareness activities, as well as increased professional and consulting fees associated with being a public company.

Comparison of the nine months ended September 30, 2018 and 2017

The following table summarizes our results of operations for the nine months ended September 30, 2018 and 2017, together with the changes in those items in dollars and as a percentage:

	Nine Months Ended September 30,		Change	
	2018	2017	\$	%
(in thousands)				
Statement of Operations Data:				
Operating Expenses:				
Research and development	\$ 31,575	\$ 16,241	\$ 15,334	94 %
Selling, general, and administrative	19,691	5,188	14,503	280 %
Total operating expenses	51,266	21,429	29,837	139 %
Loss from operations	(51,266)	(21,429)	(29,837)	139 %
Other income (loss)	2,709	(1,749)	4,458	NM %
Net loss and comprehensive loss	\$ (48,557)	\$ (23,178)	\$ (25,379)	109 %

Research and development expense. Research and development expense increased by \$15.3 million to \$31.6 million in 2018 from \$16.2 million in 2017, an increase of 94%. The increase was primarily due to the \$4.4 million non-cash expense related to the license acquired from Takeda for RM-853, a \$1.0 million milestone expense associated with the license agreement with Ipsen, an increase of \$3.9 million of employee related costs due the hiring of additional clinical and development personnel during the second half of 2017 and throughout 2018, and an increase of \$1.5 million related to the creation of our US Medical Science Liaison field force. We also had an increase of \$1.4 million related to genetic sequencing efforts designed to improve identification of patients with MC4 pathway deficiencies as well as supplemental work related to our future NDA for setmelanotide, a \$1.2 million increase related to an increase in patient visits and the number of investigator sites for new and existing clinical trials and an increase of \$1.0 million related to quality and validation consulting services within our CMC group.

Selling, general and administrative expense. Selling, general and administrative expense increased by \$14.5 million to \$19.7 million in 2018 from \$5.2 million in 2017, an increase of 280%. The increase was primarily due to an increase of \$3.7 million in employee related costs due to the hiring of additional support personnel, and an increase of \$5.4 million for the development and building of our commercial organization to drive patient identification and consulting services supporting our disease awareness activities, an increase of \$1.8 million related to marketing costs for our global launch and brand awareness programs and an increase of \$2.1 million in professional and consulting fees related to administrative infrastructure and costs associated with being a public company.

Liquidity and Capital Resources

As of September 30, 2018, our existing cash and cash equivalents and short-term investments were approximately \$272.4 million.

Cash flows

The following table provides information regarding our cash flows for the nine months ended September 30, 2018 and 2017:

	Nine Months Ended September 30,	
	2018	2017
(in thousands)		
Net cash provided by (used in):		
Operating activities	\$ (41,073)	\$ (21,575)
Investing activities	(99,423)	1,407
Financing activities	164,533	41,542
Net increase in cash, cash equivalents and restricted cash	\$ 24,037	21,374

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 \$41.1 million for the nine months ended September 30, 2018 and consisted primarily of a net loss of \$39.5 million adjusted for non-cash items, which consisted of the non-cash research and development license expense for RM-853, stock-based compensation, depreciation and amortization and deferred rent expense. The change in operating assets and liabilities reflected a total use of cash of approximately \$1.9 million for an increase in prepaid expenses associated with our CROs.

Net cash used in operating activities was \$21.6 million for the nine months ended September 30, 2017, and consisted primarily of a net loss of \$19.6 million adjusted for non-cash items, which consisted of stock-based compensation, depreciation and amortization, 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 \$1.9 million mainly for deferred issuance costs and prepaid expenses.

Net cash provided by (used in) investing activities

Net cash used by investing activities for the nine months ended September 30, 2018 relates to the net purchases of short-term investments of \$99.1 million.

Net cash provided by investing activities for the nine months ended September 30, 2017 relates to the net maturities of short-term investments of \$1.4 million.

Net cash provided by financing activities

Net cash provided by financing activities was \$164.5 million for the nine months ended September 30, 2018, which represents net proceeds from our public offering in June 2018 and proceeds from the exercise of stock options.

Net cash provided by financing activities was \$41.5 million for the nine months ended September 30, 2017, which represents the net proceeds from the first and second tranche of our issuance of series A preferred stock in January 2017 and August 2017, respectively.

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 also expect to incur additional costs associated with operating as a public company.

We expect that our existing cash and cash equivalents will enable us to fund our operating expenses into the second half of 2020. 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;

[Table of Contents](#)

- the obligations owed to Ipsen Pharma S.A.S., or Ipsen, Camurus AB, or Camurus, and Takeda, pursuant to our license agreements;
- 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. In October 2017 we completed our IPO in which we received net proceeds of \$125.7 million. In June 2018 we completed another public offering of our common shares in which we received net proceeds of \$163.0 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.

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, Camurus and Takeda, 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

[Table of Contents](#)

\$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 this formulation of setmelanotide. Under the terms of the Takeda license agreement, assuming that RM-853, is successfully developed, receives regulatory approval and is commercialized, Takeda may receive aggregate payments of up to \$140.0 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 Takeda license agreement are for milestones that may be achieved no earlier than first commercial sale of the RM-853.

In August 2018, we amended our existing Lease Agreement for our head office facility in Boston, Massachusetts. The new lease term will commence in August 2019 and has a term of six years with a five-year renewal option to extend the lease.

Future minimum payments under the Lease Agreement, as amended, are as follows:

	Operating Lease
2018	\$ 75
2019	425
2020	786
2021	802
2022	818
Thereafter	2,187
Total	\$ 5,093

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.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risk related to changes in interest rates. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments, including cash equivalents, are in the form, or may be in the form of, money market funds or marketable securities and are or may be invested in U.S. Treasury and U.S. government agency obligations. Due to the short-term maturities and low risk profiles of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our investments.

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

JOBS Act

In April 2012, the Jumpstart our Business Startups Act of 2012, or 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 of 1933, as amended, or 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.

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) December 31, 2022, (2) the last day of the fiscal year (a) in which we have total annual gross revenue of at least \$1.07 billion, or (b) 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 (3) the date on which we have issued more than \$1.0 billion in non-convertible debt securities during the prior three-year period.

Item 4. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, are controls and other procedures designed to ensure that information required to be disclosed in reports filed or submitted under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified by the rules and forms promulgated by the SEC. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that such information is accumulated and communicated to management, including the chief executive officer and the chief financial officer, as appropriate, to allow timely decisions regarding required disclosure.

In connection with the preparation of this Quarterly Report on Form 10-Q, we completed an evaluation, as of September 30, 2018, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, as to the effectiveness of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act).

It should be noted that any system of controls, however well designed and operated, can provide only reasonable, and not absolute, assurance that the objectives of the system will be met. In addition, the design of any control system is based in part upon certain assumptions about the likelihood of future events. Based upon the evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of September 30, 2018, our disclosure controls and procedures were effective at a reasonable assurance level.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the period covered by this report that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II - OTHER INFORMATION

Item 1. Legal Proceedings.

We are not currently a party to any material legal proceedings.

Item 1A. Risk Factors

Our operations and financial results are subject to various risks and uncertainties, including those described below, which could adversely affect our business, financial condition, results of operations, cash flows, and the trading price of our common stock. Additional risks and uncertainties that we currently do not know about or that we currently believe to be immaterial may also impair our business. You should carefully consider the risks described below and the other information in this Quarterly Report on Form 10-Q, including our unaudited consolidated financial statements and the related notes thereto, and “Management’s Discussion and Analysis of Financial Condition and Results of Operations”.

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. See “Part I, Item 2. Management’s Discussion and Analysis of Financial Condition and Results of Operations—Corporate Background and Distribution.”

Our net loss and comprehensive losses were \$17.7 million, \$10.0 million, \$48.6 million and \$23.2 million for the three and nine months ended September 30, 2018 and 2017, respectively. As of September 30, 2018, we had an accumulated deficit of \$159.1 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. We also 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 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;

[Table of Contents](#)

- 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.

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 our available cash resources 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. In October 2017 we completed our initial public offering, or IPO, of 8,107,500 shares of common stock at an offering price of \$17.00 per share, which included the exercise in full by the underwriters of their option to purchase up to 1,057,500 additional shares of common stock. We received gross proceeds of approximately \$137.8 million, before deducting underwriting discounts, commissions and offering related transaction costs. On June 25, 2018, we completed a public offering of 6,591,800 shares of common stock at an offering price of \$26.42 per share, which included the exercise in full by the underwriters of their option to purchase up to 859,800 additional shares of common stock. We received gross proceeds of approximately \$174.2 million, before deducting underwriting discounts, commissions and offering related transaction costs. As of September 30, 2018, our cash and cash equivalents and short-term investments were approximately \$272.4 million. We expect our existing cash and cash equivalents will enable us to fund our operating expenses into the second half of 2020. 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 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 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 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 information we have included in this Quarterly Report on Form 10-Q 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.

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 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 believe we have also demonstrated preliminary proof of concept in a Phase 2 clinical trial for Alström syndrome. 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 and Alström 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.

We have and will continue to 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 may not provide opportunities for acceleration and 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 contrast, 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. However, we have completed the key toxicology studies that the United States Food and Drug Administration, or the FDA, will require for our first approval, and which we believe the European Medicines Agency, or EMA, will require for authorization, 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, the FDA has agreed to permit us to defer carcinogenicity studies until after approval of an NDA for setmelanotide. Accordingly, we believe that we will be able to defer the submission of all carcinogenicity studies until after we receive regulatory approval to market setmelanotide in the U.S. While we believe this also to be true for the EMA, the EMA has not yet provided firm guidance on the need for carcinogenicity studies and accordingly, there can be no guarantee that we will be able to achieve this deferral which could impact the timing of any potential European Union, or EU, approval.

In addition to the foregoing issue, the FDA has requested that in our chronic rat and monkey studies we re-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 monkey 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, or PEG, vehicle in the product, rather than setmelanotide itself. A similar question was raised by the competent authorities in France, in connection with the use of PEG in products for younger pediatric indications, and in discussion of our Pediatric Investigational Plan, or PIP. Based on this, we performed this re-assessment, which confirmed that no additional findings were present in any monkey tissues, but which did find a very small number of rats with vacuolated epithelial cells, or brain surface lining cells, in the choroid plexus of minimal severity that also appeared to be related to the PEG vehicle. We do not believe these findings raise any important safety concerns, in part because of the minimal severity, the localization of these aggregates, the lack of any adverse histopathological changes, and the lack of findings in other tissues. However, neither the FDA nor regulatory agencies in the EU has indicated that they agree with our position. In addition, we anticipate the EMA may request additional mechanistic studies to better understand these findings. It is also possible the FDA may require us to reflect these findings in the toxicological portion of the product labeling, and this may delay study in the youngest pediatric patients in some EU member states, such as France.

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 clinical 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.

Based on clinical epidemiology, 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;

[Table of Contents](#)

- 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 (body mass index, or 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%.

- *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
 - our belief 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
 - our belief 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 EU are at least as large as those in the United States. However, we do not have comparable epidemiological data from the EU 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 have developed a patient registry for diagnosed patients with POMC deficiency and LepR deficiency (and other genetic disorders of obesity) 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. Our initial 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. Our continued investigations support that the genetic epidemiological estimates are larger than the clinical epidemiological estimates, but we will likely need to reconcile the scientific definition of mutations with the regulatory definition.

We believe the separate analyses that we have completed using clinical epidemiology and genetic epidemiology provide a robust range of patient population estimates for these rare disorders. However, to be conservative, we reference the clinical epidemiology figures in our descriptions of our target indications.

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 twelve years of age and older in our trials, and have started treating patients six to eleven years of age. Our aim is to gain regulatory approval and labeling for patients six years of age and older. We have received permission from the FDA and other equivalent competent authorities in the EU member states to enroll these younger patients, aged six to eleven, in our pivotal trials. However, there may be issues that preclude the ultimate approval and labeling including, but not limited to, potential disagreement on dose titration, or delivery methods for small doses, or the suitability of patient reported outcomes in younger patients, the clinical endpoints in rapidly growing 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, and may look to new formulations, such as our once-weekly formulation, as being more suitable to younger pediatric patients. We also may not have one-year clinical data in six to eleven year old patients at the time of the POMC NDA filing, if we begin recruiting six to eleven year old patients into our pivotal trials, though we can provide one-year clinical data when it becomes available. We cannot predict if the FDA or other equivalent competent authorities in the EU member states will approve setmelanotide in younger pediatric patients, nor provide an estimate for the timing for approval, if any, for the use of setmelanotide for such patients. Furthermore, if the FDA or other equivalent competent authorities in the EU member states do 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 twelve and older.

While we currently have no knowledge of competitors developing product candidates intended to treat upstream MC4 pathway deficiencies, other than Prader-Willi-Syndrome, 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, and could impact our commercial success.

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 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 advancing an ongoing pivotal Phase 3 clinical trial for setmelanotide for POMC deficiency obesity. We completed Phase 2 clinical trials for setmelanotide for LepR deficiency obesity, and are currently advancing an ongoing pivotal Phase 3 clinical trial for setmelanotide in LepR deficiency obesity. These trials are overlapping in timing and duration and we plan to discuss with the FDA and other regulatory agencies, and will likely file concurrent NDAs for these two indications, which would have an impact on NDA timing and complexity.

We believe we have demonstrated proof of concept in Bardet-Biedl syndrome and Alström syndrome, and are in ongoing discussions with the FDA to plan a pivotal Phase 3 clinical trial in Bardet-Biedl syndrome, likely combined with a pivotal Phase 3 clinical trial in Alström syndrome, that we anticipate we can initiate in 2018. We believe that the combined Bardet-Biedl syndrome and Alström syndrome Phase 3 pivotal trial may be somewhat different in design than those for POMC and LepR deficiency obesity, respectively, most likely due to the larger available patient population for inclusion in a clinical study. There may be other changes as well, as our feedback from the FDA is preliminary, and we have not yet consulted with the European regulatory agencies. We have also initiated Phase 2 clinical trials for POMC and other MC4 pathway heterozygous deficiency obesities, and POMC epigenetic disorders. We anticipate that the Phase 2 clinical trials in these indications may be more complex than those for which we have achieved proof of concept.

Successful completion of such Phase 3 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. While we believe that a transition from proof of concept to pivotal trials may be more straight-forward for Alström syndrome, it is likely that Phase 2 clinical trials will be longer and more complex for POMC heterozygous deficiency obesity and POMC epigenetic disorders, due to the greater variety of clinical presentation in those conditions.

[Table of Contents](#)

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 successful 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 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, as well as the lack of alternatives to these sites which have already-diagnosed patients;
- 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 in 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;
- 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;

[Table of Contents](#)

- 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 enrollment for our clinical trials of Bardet-Biedl syndrome and Alström syndrome due to the fact that we have not yet completed our discussions with the FDA regarding clinical trials for these indications, do not know if the FDA will disagree with our proposed Phase 3 clinical trial design;
- potential difficulties in defining the indication for Bardet-Biedl syndrome, as there may be discrepancies between the syndromic, or clinical definition of the syndrome, and the genetic confirmation of the indication;
- lack of ability to predict which patients will have the most consistent responses to setmelanotide in the patients with rare genetic disorders of obesity that we are studying, as not all patients may show robust, or even any response to treatment;
- 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 the need to study larger numbers of patients than for our first two indications, 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;
- 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; and
- lack of a complete understanding of the absorption, distribution, metabolism and excretion of setmelanotide, or an incomplete set of clinical pharmacology studies to support labeling.

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. We believe we can apply the same guidance to our future pivotal trials in other indications. 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 trials 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, or we experience difficulties in the methods of statistical analysis for hunger and hyperphagia, 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 adverse events noted at somewhat greater rates numerically for setmelanotide compared to placebo across the clinical program, which include fatigue and related symptoms, diarrhea, arthralgia, back pain and headache, though most investigators reported these effects to be unrelated to setmelanotide.

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 receptor mediated effects include darkening of skin blemishes, such as freckles and moles, and hair color change. The cosmetic effects are not tolerated by all patients, as a small number of patients have withdrawn from treatment due to tanning. 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 receptor mediated effects may also carry risks. The long-term impact of MC1 receptor 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. 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 ten other serious adverse events in the full development program, in addition to the serious adverse event described above: seven others on setmelanotide, mostly from open label trials, including left arm numbness, influenza immunization reaction, pancreatitis secondary to pre-existing gallstones, pneumonia, hypoglycemia due to acute adrenal insufficiency, due to non-compliance with hydrocortisone regimen, a depressive episode with elective admission to a psychiatry ward in a patient with history of depression and who continued on treatment, and rotavirus-related gastroenteritis. There were also three serious adverse events during treatment with placebo, consisting of biliary dyskinesia, severe groin strain, and pelvic inflammatory disease. None of these serious adverse events was considered related to setmelanotide treatment. In addition, there has been a serious adverse event with respect to a study participant in our Phase 3 pivotal study for LEPR deficiency obesity who died in a fatal motor vehicle accident, in which

[Table of Contents](#)

the driver lost control, and our study participant was a passenger. This was determined not to be related to setmelanotide treatment.

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, lipodystrophy and other indications. It is possible that the underlying conditions in these patients, such as congestive heart failure, pancreatitis, and potentially other conditions 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 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 and LepR 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 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 and LepR 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 POMC deficiency obesity, LepR deficiency obesity, Bardet-Biedl syndrome and Alström syndrome, the FDA may rescind the Breakthrough Therapy 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." A 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. The initial Phase 1 pharmacokinetic data from healthy obese volunteers supports once-weekly dosing, but has only been administered for short durations. It is possible that the tolerability profile and/or pharmacokinetics in patients will not be similar to that of healthy obese volunteers, making development of this product more complex. In addition, we have not consulted with regulatory agencies about the path for approval of the once-weekly formulation, and, accordingly, we cannot estimate the time, cost, and probability of success for approval. The Camurus formulations have also not been approved for any product at this time, which further complicates our understanding for the path to approval.

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 previously 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.

Although the FDA had previously advised us that an LDT is sufficient for identifying patients in our clinical trials, the agency also previously 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. More recent communications from the FDA have increased the potential for a need for a companion diagnostic device. *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 device 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 also are discussing with the FDA the specific mutations, or variants, that will define each indication for which we intend to seek approval. Our efforts have focused on loss-of-function variants that effectively inactivate the genes in the MC4 pathway, and we have proposed rules to define these variants for approval, and which can be used to categorize new variants as they are identified. The FDA has asked us to consider an alternative approach for categorizing and validating these variants that has been used for other diagnostics, and we are likely to agree.

In addition, we intend to apply genetic tests to address goals beyond seeking FDA approval of setmelanotide, including supporting efforts to explore and expand the diagnosis of patients with genetic causes of obesity, and to assist in building awareness of these illnesses. As such, we may develop or work with partners to develop additional genetic tests in the area of genetic obesity, including panels that may study a larger number of genes. There are many factors that might influence the success of these efforts, which could be impactful on our commercial efforts, including the cost, analytical methods, and the ability to provide clinical and diagnostic information to patients and doctors.

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

We have only one product candidate in clinical development and may seek to identify and develop additional product candidates for clinical development, 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 continuing to evaluate setmelanotide in another Phase 2 trial. We do not know the probability that we will be able to succeed in this additional Phase 2 trial and/or 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 for this, and many other reasons, 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.

In addition, we have begun a program for a new mechanism that may have therapeutic effects in PWS, but this program is in preclinical development, and our candidate, RM-853, may not succeed in completing the pre-IND studies needed to proceed to clinical trials, or may fail in early Phase 1 studies due to unfavorable safety, pharmacokinetics or for other reasons. The hypothesis supporting the therapeutic effects of this mechanism is also based on limited clinical and preclinical information, and even if RM-853 were to progress to a Phase 2 proof of concept study, it is unclear if there will be safety and efficacy to support proceeding further in development.

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 twelve 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 EU, 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 setmelanotide from lower priced products in foreign countries that have placed price controls on pharmaceutical products.

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, Spain 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 EU 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 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 upstream 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 and any equivalent laws in foreign countries. 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;

[Table of Contents](#)

- distraction of management's attention from our primary business;
- loss of revenue; and
- 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, and IRBs. 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 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 may 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.

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;
- 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. All but a few 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. Although subsequent to our response, the third party has allowed all the remaining 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 or choose 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 have licensed our rights to RM-853 from Takeda Pharmaceutical Company Limited, or Takeda. Our license with Takeda imposes various obligations on us, and provides Takeda the right to terminate the license in the event of our material breach of the license agreement, if we voluntarily or involuntarily file for bankruptcy, or for our bringing an action seeking to have a Takeda license patent right declared invalid. Termination of our license from Takeda would result in our inability to use the licensed intellectual property.

Among other obligations under our agreement with Takeda, Takeda has a right of first negotiation under certain circumstances to sublicense the assets we acquired from Takeda in the territory of Japan. This right of first negotiation remains in effect until the earlier of five years from the date of the agreement, consummation of a change in control, or sublicense to a third party. This may delay or limit our ability to enter into certain transactions with respect to this product candidate.

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 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, and for which we expect to initiate Phase 3 clinical development in Bardet-Biedl syndrome and Alström syndrome in 2018, 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 our existing cash resources. 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 of 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 the competent authorities in such countries. We have two Phase 3 clinical trials underway, one each for the treatment of POMC deficiency obesity and LepR deficiency obesity, and plan to initiate a third combined Phase 3 trial for Bardet-Biedl syndrome and Alström syndrome by the end of 2018. 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 has provided clear advice in the past, but could at any time alter its previous advice on many aspects of the trial—the small size, the primary and key secondary endpoints, 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 six or over—all of which may impact the timing and ability to obtain FDA approval. For example, the FDA asked us in December 2017 to switch the order of our primary and key secondary endpoints for weight in our POMC deficiency Phase 3 protocol. While this might be favorable as the new primary endpoint has increased statistical power—the ability to produce a positive study result—this change occurred after the Phase 3 trial had started and may result in additional complexities such as more attention to compliance and retention. There are other aspects of the trial for which we 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 received FDA comments that indicate the Phase 3 program for LepR deficiency can be similar to POMC deficiency, but we have not yet discussed with the FDA the protocol for a Phase 3 program for LepR deficiency obesity in detail. Therefore, the timeline for enrollment, availability of data, and cost of conducting such trials are less certain, and could be less favorable than those applicable to the POMC deficiency obesity program. Similarly, the preliminary FDA advice on the design of the Bardet-Biedl syndrome and Alström syndrome combined clinical Phase 3 study could, at any time, be altered by the FDA, including for example, the size of the trial, the type and importance of endpoints, the length of the trial, the ability to combine the two indications, the inclusion of pediatric patients and pediatric efficacy endpoints, and the design for any placebo-controlled aspect of the trial.

In addition, the FDA and other equivalent competent authorities in foreign jurisdictions will expect for there to be little, or 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 indications. 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 will determine in our own judgment if a non-pivotal trial meets “proof of concept” in each of these indications. There is no certainty that the FDA, other competent authorities, or outside investors will agree with our determination, which might have an impact on the ability to transition to Phase 3 studies.

In the EU we are currently conducting the Phase 3 clinical trial RM-493-012 in Germany, France, Belgium, and the United Kingdom for POMC deficiency obesity. We are also conducting this trial in Canada. 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

[Table of Contents](#)

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 also advised, however, that we need to consider whether full approval or approval under conditional or exceptional circumstances would be the most appropriate pathway for application for POMC deficiency obesity.

In the EU we are currently conducting the Phase 3 clinical trial RM-493-015 in Germany, France, Netherlands, and the United Kingdom, for LepR deficiency obesity. We are also conducting this study in the United States. We have not obtained EMA scientific advice for the LepR deficiency indication, nor have we obtained EMA scientific advice for the Bardet-Biedl syndrome or Alström syndrome indications.

Given the orphan status of setmelanotide for the treatment of POMC deficiency in the EU the marketing authorization application for a POMC deficiency obesity indication will likely be submitted via the centralized procedure. We will also have to obtain orphan status in the EU for LepR deficiency obesity. In addition, we have submitted a pediatric investigation plan, or PIP, for setmelanotide to the EMA Pediatric Committee, or PDCO, in 2017. On April 27, 2018, the PDCO adopted an opinion accepting the PIPs for setmelanotide in the treatment of appetite and general nutritional disorders, including the deferral and the waiver requested by us.

We cannot assure you that the clinical trials we are conducting in the EU 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 or 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 and Phase 3 clinical trials such that if the clinical trials are successful, we can file NDAs for POMC deficiency obesity and LepR deficiency obesity in the United States by 2019 or early 2020. 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 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;

[Table of Contents](#)

- 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 jurisdictions 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 jurisdictions 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 may 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;
- 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 EU 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 EU, commonly referred to as Brexit. On March 29, 2017, the country formally notified the EU 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 EU directives and regulations, the withdrawal of the United Kingdom from the EU could materially impact the regulatory regime with respect to the approval of setmelanotide in the United Kingdom or the EU. 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 EU 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 EU 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 changes, 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 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 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 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.

Current 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.

[Table of Contents](#)

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 of 2010, 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 product candidates 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;
- 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, for example, 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 have occurred in the 115th U.S. Congress and under the Trump administration. For example, the Tax Cuts and Jobs Act enacted on December 22, 2017, eliminated the shared responsibility payment for individuals who fail to maintain minimum essential coverage under section 5000A of the Internal Revenue Code of 1986, as amended, or the Code, commonly referred to as the individual mandate, beginning in 2019. Further, in the Bipartisan Budget Act of 2018, the Medicare Part D coverage gap discount program was revised to increase drug manufacturers' discount levels under the program. Additional legislative changes to and regulatory changes under the ACA remain possible, but the nature and extent of such potential additional changes are uncertain at this time. We expect that the ACA, as currently enacted or as it may be amended in the future, and other healthcare reform measures that may be adopted in the future, could have a material adverse effect on our industry generally and on our ability to successfully commercialize our product candidates, if approved.

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, other Phase 1 trials, 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 EU, 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 EU. The applicable laws at EU 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 EU 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 be 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, 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, including, for example, Section 5 of the FTC Act, govern the collection, use, disclosure and protection of health-related and other personal information.
- 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 investment 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 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. Some states restrict the ability of manufacturers to offer co-pay support to patients for certain prescription drugs. Other states and cities require identification

or licensing of sales representatives. 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. Various state and federal regulatory and enforcement agencies continue actively to investigate violations of health care laws and regulations, and the United States Congress continues to strengthen the arsenal of enforcement tools. Most recently, the Bipartisan Budget Act of 2018 increased the criminal and civil penalties that can be imposed for violating certain federal health care laws, including the Anti-Kickback Statute. 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, imprisonment, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, 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. Some of these laws and related risks are described under the risk factor *"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"* of this Quarterly Report on Form 10-Q.

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, for example, 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, including, for example, 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 EU, the collection and use of personal health data is governed by the provisions of the General Data Protection Regulation, or GDPR. The GDPR became effective on May 25, 2018, repealing the Data Protection Directive and increasing our responsibility and liability in relation to the processing of personal data of EU subjects.

The GDPR, together with the national legislation of the EU member states governing the processing of personal data, 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 provided to the individuals, the transfer of personal data out of the EU, security breach notifications, security and confidentiality of the personal data, and imposition of substantial potential fines for breaches of the data protection obligations. Data protection authorities from the different EU member states may interpret the GDPR and national laws differently and impose additional requirements, which add to the complexity of processing personal data in the EU. Guidance on implementation and compliance practices are often updated or otherwise revised.

With respect to the transfer of personal data out of the EU, the GDPR provides that the transfer of personal data to countries that are not considered by the European Commission to provide an adequate level of data protection, including the United States, is permitted only on the basis of complying with specific legal steps.

The judgment by the Court of Justice of the European Union in Case C-362/14 Maximilian 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 EU 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 EU to the United States.

However, in October 2016, three French digital rights advocacy group, La Quadrature du Net, French Data Network and the Fédération FDN, 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-738/16). The case is 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 EU 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 GDPR.

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. In particular, our failure to comply with our obligations under the GDPR, including any failure to adopt measures to ensure

that we can continue to conduct the data processing activities that we have initiated in the EU before the GDPR entered into application could adversely impact the validity of data generated in our studies.

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 EU 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 EU. The procedure involves a two-year negotiation period in which the United Kingdom and the EU 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 EU. 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 EU. This includes the laws and regulations that will apply as the United Kingdom determines which EU 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 EU is the requirement that the applicant is established in the EU. Following withdrawal of the United Kingdom from the EU, 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 EU 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 EU 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 EU. 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.

Risks Related to Preclinical Development and Clinical Development of RM-853

We have assumed sole responsibility for the global product development and commercialization of RM-853, which may distract our management team from pursuing regulatory approval of setmelanotide, and we may never complete preclinical development of RM-853 or file an IND with the FDA. Many of the risks we have faced in preclinical development and in clinical development of setmelanotide will also exist in preclinical development of RM-853 and clinical development, should we ever enter into clinical development of RM-853

In March 2018 we entered into a license agreement with Takeda Pharmaceutical Company Limited, which we refer to as Takeda, to develop and commercialize T-3525770, now known as RM-853. RM-853 is a potent, orally available ghrelin o-acyltransferase, or GOAT, inhibitor currently in preclinical development for PWS. Under the terms of the license agreement, we assumed sole responsibility for the global product development and commercialization of RM-853. This relationship may distract our management team from clinical development of setmelanotide and may require us to expend financial and other resources. PWS is a complex disease and companies have had difficulties in developing new therapies for PWS. In addition, many of the risks we have faced in preclinical development and in clinical development of setmelanotide will also exist in preclinical development of RM-853 and clinical development, should we ever enter into clinical development of RM-853, including, but not limited to:

- RM-853 may not succeed in preclinical toxicology studies or may not be accepted by the FDA under an IND;
- results from preclinical studies may not be predictive of later clinical trials of RM-853;
- Phase 1 studies may show that RM-853 has a significant toxicities or pharmacokinetics not supportive of proceeding in development;
- failures or delays in the commencement or completion of preclinical studies or clinical trials could result in increased costs to us and could delay, prevent or limit our ability to generate revenue and continue our business;
- RM-853 could cause undesirable side effects that could result in significant negative consequences, including the inability to enter clinical development or receive regulatory approval;
- experience by others suggest that PWS patients are high risk for adverse experiences and for this, and many other reasons, clinical trials in that population are extremely challenging;
- other risks related to regulatory approval, and if ever received, marketing and commercialization of RM-853;
- potential product liability exposure;
- an inability to protect our intellectual property related to RM-853;
- risks related to our dependence on third parties, including in manufacturing RM-853 and conducting preclinical studies and clinical trials of RM-853;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements; and
- competition from other therapies in development for the treatment of PWS may result in reduced availability of patients for our clinical studies, the possible requirement to achieve clinical meaningful efficacy above any treatment that is approved prior to RM-853, and the potential for increased scrutiny from payers related to the relative benefit of RM-853 versus other therapies should they be approved prior to RM-853.

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, Simon Kelner, our Chief Human Resources Officer, Murray Stewart, M.D., our Chief Medical Officer and Lex H.T. Van der Ploeg, Ph.D., our Chief Scientific Officer. We have employment agreements with these individuals 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.

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 must establish and maintain effective disclosure and financial controls. We will need to continue 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

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant influence over matters subject to stockholder approval.

Based on the number of shares outstanding as of September 30, 2018, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately 43% of our voting stock. These stockholders will have significant influence over matters requiring stockholder approval. For example, these stockholders will significantly influence elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders.

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.

An active market for our common stock may not be maintained.

Our stock only began trading on the Nasdaq Global Market in October 2017 and we can provide no assurance that we will be able to maintain an active trading market on the Nasdaq Global Market or any other exchange in the future. If an active market for our common stock is not maintained, it may be difficult for our stockholders to sell shares without depressing the market price for the shares or at all. An inactive market may also impair our ability to raise capital by selling

shares and may impair our ability to acquire other businesses, applications or technologies using our shares as consideration.

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

The market price for our common stock has been volatile and may continue to 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;

[Table of Contents](#)

- 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 have broad discretion in how we use the proceeds from our IPO and June 2018 public offering. We may not use these proceeds effectively, which could affect our results of operations and cause our stock price to decline.

We have considerable discretion in the application of the net proceeds from our IPO and June 2018 public offering. We intend to continue to use the net proceeds 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 and Alström 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 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. 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 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 Code, a corporation is generally allowed a deduction for net operating losses, or NOLs, carried over from a prior taxable year. Under the Code, we can carry forward certain NOLs of our subsidiaries to offset future taxable income, if any, until such losses are used or, for NOLs arising in taxable years ending on or before December 31, 2017, until such NOLs expire. NOLs arising in taxable years ending after December 31, 2017 are not subject to expiration. NOLs arising in taxable years beginning after December 31, 2017 may only be used to offset up to 80% of the corporation's taxable income computed without taking into account NOL deductions. Other unused tax attributes, such as research tax credits may also be carried forward to offset future taxable income, if any, until such credits are used or expire. As of December 31, 2017, we had approximately \$73.1 million and \$3.8 million of unused federal and state carryforwards of NOLs, respectively, and approximately \$1.9 million and \$0.5 million of unused federal and state carryforwards of tax credits, respectively. Additionally, as of December 31, 2017, we had federal orphan drug credits related to qualifying research of \$2.3 million.

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 our IPO may result in a limitation under Code 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.

Substantial future sales or perceived potential sales of our common stock in the public market could cause the price of our common stock to decline significantly.

Sales of our common stock in the public market, or the perception that these sales could occur, could cause the market price of our common stock to decline significantly. As of September 30, 2018, we have 34,382,525 shares of common stock outstanding.

The holders of approximately 12.0 million shares of our common stock, or approximately 35% of our total outstanding common stock as of September 30, 2018, are entitled to rights with respect to the registration of their shares under the Securities Act, subject to vesting schedules. 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 trading price of our common stock.

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) December 31, 2022, (2) the last day of the fiscal year (a) in which we have total annual gross revenue of at least \$1.07 billion, or (b) 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 (3) the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period.

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.

If securities or industry analysts do not continue to 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. If we lose securities or industry analysts coverage of our company, the trading price for our stock would be negatively impacted. 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.

We will continue to incur substantial costs as a result of operating as a public company, and our management will continue 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 continue to incur significant legal, accounting and other expenses. 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 continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will continue to increase our legal and financial compliance costs and make some activities more time-consuming and costly.

We 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.

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.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds.

Unregistered Sales of Equity Securities

None.

[Table of Contents](#)

Use of Proceeds

We issued shares of our common stock on the Nasdaq Global Market on June 25, 2018. The offer and sale of all the shares in the public offering were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-225700), which was declared effective by the SEC on June 20, 2018.

There has been no material change in the planned use of proceeds from our public offering as described in the Prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act on June 20, 2018.

Repurchased of Shares or of Company Equity Securities

None.

Item 3. Defaults Upon Senior Securities

Not applicable.

Item 4. Mine Safety Disclosure

Not applicable.

Item 5. Other Information

None

[Table of Contents](#)

Item 6. Exhibits

Exhibit Number	Exhibit Description	Incorporated by Reference		
		Form	Date	Number
10.1	Second Amendment to Lease, dated August 6, 2018.	8-K	8/9/2018	10.1
31.1*	Certification of the Chief Executive Officer, as required by Section 302 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. 1350).			
31.2*	Certification of the Chief Financial Officer, as required by Section 302 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. 1350).			
32.1*	Certification of the Chief Executive Officer, as required by Section 906 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. 1350).			
32.2*	Certification of the Chief Financial Officer, as required by Section 906 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. 1350).			
101.INS*	XBRL Instance Document.			
101.SCH*	XBRL Taxonomy Extension Schema Document.			
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document.			
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document.			
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document.			
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document.			

* Filed or furnished herewith.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

RHYTHM PHARMACEUTICALS, INC.

Dated: November 9, 2018

By: /s/ Keith M. Gottesdiener
Name: Keith M. Gottesdiener
Title: Chief Executive Officer, President and Director
(Principal Executive Officer)

Dated: November 9, 2018

By: /s/ Hunter Smith
Name: Hunter Smith
Title: Chief Financial Officer and Treasurer
(Principal Financial and Accounting Officer)

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Keith M. Gottesdiener, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Rhythm Pharmaceuticals, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 9, 2018

/s/ Keith M. Gottesdiener

Name: Keith M. Gottesdiener

Title: Chief Executive Officer, President and Director
(Principal Executive Officer)

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Hunter Smith, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Rhythm Pharmaceuticals, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 9, 2018

/s/ Hunter Smith

Name: Hunter Smith

Title: Chief Financial Officer and Treasurer
(Principal Financial And Accounting Officer)

**CERTIFICATION OF CHIEF EXECUTIVE OFFICER
PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

I, Keith M. Gottesdiener, certify pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge, the Quarterly Report on Form 10-Q of Rhythm Pharmaceuticals, Inc. for the fiscal quarter ended September 30, 2018 fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934 and the information contained in such Form 10-Q fairly presents, in all material respects, the financial condition and results of operations of Rhythm Pharmaceuticals, Inc.

/s/ Keith M. Gottesdiener

Name: Keith M. Gottesdiener

Title: Chief Executive Officer, President and Director
(Principal Executive Officer)

November 9, 2018

**CERTIFICATION OF CHIEF FINANCIAL OFFICER
PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

I, Hunter Smith, certify pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge, the Quarterly Report on Form 10-Q of Rhythm Pharmaceuticals, Inc. for the fiscal quarter ended September 30, 2018 fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934 and the information contained in such Form 10-Q fairly presents, in all material respects, the financial condition and results of operations of Rhythm Pharmaceuticals Inc.

/s/ Hunter Smith

Name: Hunter Smith

Title: Chief Financial Officer and Director
(Principal Financial and Accounting Officer)

November 9, 2018
