# 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, 2017**
**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** | **46-2159271** |
|---|---|
| (State or other jurisdiction of incorporation or organization) | (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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post 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 ☒ (Do not check if a smaller reporting company) | 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 10, 2017 was 27,284,140.

**RHYTHM PHARMACEUTICALS, INC.**

**FORM 10-Q**

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**PART I – FINANCIAL INFORMATION**

**Item 1. Financial Statements.**

**Rhythm Pharmaceuticals, Inc.**

**Condensed Balance Sheets**

**(in thousands, except share and per share data)**

| | (Unaudited) September 30, 2017 | December 31, 2016 |
|---|---|---|
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 27,914 | $ 6,540 |
| Short-term investments | 2,501 | 3,997 |
| Prepaid expenses and other current assets | 1,621 | 638 |
| Total current assets | 32,036 | 11,175 |
| Property, plant and equipment, net | 845 | 930 |
| Deferred issuance costs | 1,698 | 9 |
| Restricted cash | 225 | 225 |
| Total assets | $ 34,804 | $ 12,339 |
| **Liabilities, convertible preferred stock and stockholders' equity (deficit)** | | |
| Current liabilities: | | |
| Accounts payable | $ 2,271 | $ 1,895 |
| Due to related party | — | 105 |
| Deferred rent | 81 | 76 |
| Accrued expenses and other current liabilities | 3,108 | 2,655 |
| Total current liabilities | 5,460 | 4,731 |
| Long-term liabilities: | | |
| Deferred rent | 250 | 311 |
| Total liabilities | 5,710 | 5,042 |
| Commitments and contingencies | | |
| Preferred stock: | | |
| Series A Convertible Preferred Stock, $1.00 par value: 80,950,000 shares authorized; 80,949,999 shares issued and outstanding at September 30, 2017 and 40,000,000 shares issued and outstanding at December 31, 2016; (aggregate liquidation preference of $88,864 and $44,129 at September 30, 2017 and December 31, 2016 respectively) | 80,950 | 40,000 |
| Stockholders' equity (deficit): | | |
| Common stock, $0.001 par value: 29,919,979 shares authorized; 1,770,302 and 10,196,292 shares issued and outstanding and September 30, 2017 and December 31, 2016, respectively | 2 | 10 |
| Series A-1 Convertible Junior Preferred Stock, $0.001 par value, 78,666,209 shares authorized; 78,666,209 and no shares issued and outstanding at September 30, 2017 and December 31, 2016, respectively | 79 | — |
| Additional paid-in capital | 47,784 | 43,830 |
| Accumulated deficit | (99,721) | (76,543) |
| Total stockholders' equity (deficit) | (51,856) | (32,703) |
| Total liabilities, convertible preferred stock and stockholders' equity (deficit) | $ 34,804 | $ 12,339 |

The accompanying notes are an integral part of these financial statements

**Rhythm Pharmaceuticals, Inc.**

**Condensed Statements of Operations and Comprehensive Loss**

**(in thousands, except share and per share data)**

**(Unaudited)**

| | Three months ended September 30, | | Nine months ended September 30, | |
|---|---|---|---|---|
| | 2017 | 2016 | 2017 | 2016 |
| Operating expenses: | | | | |
| Research and development | $ 5,971 | $ 5,419 | $ 16,241 | $ 13,963 |
| General and administrative | 2,315 | 982 | 5,188 | 3,567 |
| Total operating expenses | 8,286 | 6,401 | 21,429 | 17,530 |
| Loss from operations | (8,286) | (6,401) | (21,429) | (17,530) |
| Other income (expense): | | | | |
| Revaluation of Series A Investor Instrument | (1,781) | — | (1,863) | — |
| Interest income, net | 51 | 10 | 114 | 24 |
| Total other income (expense): | (1,730) | 10 | (1,749) | 24 |
| Net loss and comprehensive loss | $ (10,016) | $ (6,391) | $ (23,178) | $ (17,506) |
| Net loss attributable to common stockholders | $ (11,429) | $ (7,191) | $ (26,963) | $ (19,902) |
| Net loss attributable to common stockholders per common share, basic and diluted | $ (1.78) | $ (0.71) | $ (3.02) | $ (1.95) |
| Weighted average common shares outstanding, basic and diluted | 6,404,254 | 10,196,292 | 8,918,389 | 10,196,292 |

The accompanying notes are an integral part of these financial statements

**Rhythm Pharmaceuticals, Inc.**

**Condensed Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)**

**(in thousands, except share and per share data)**

**(Unaudited)**

| | Series A Convertible Preferred Stock | | Common Stock | | Series A-1 Junior Preferred Stock | | Additional Paid-In Capital | Accumulated Deficit | Total Stockholders' Equity (Deficit) |
|---|---|---|---|---|---|---|---|---|---|
| | Shares | Amount | Shares | Amount | Shares | Amount | | | |
| Balance at December 31, 2015 | 40,000,000 | $ 40,000 | 10,196,292 | $ 10 | — | $ — | $ 42,662 | $ (50,671) | $ (7,999) |
| Stock compensation expense | — | — | — | — | — | — | 1,168 | — | 1,168 |
| Net loss | — | — | — | — | — | — | — | (25,872) | (25,872) |
| Balance at December 31, 2016 | 40,000,000 | 40,000 | 10,196,292 | 10 | — | — | 43,830 | (76,543) | (32,703) |
| Stock compensation expense | — | — | — | — | — | — | 1,569 | — | 1,569 |
| Issuance of common stock in connection with exercise of stock options | — | — | 152,671 | — | — | — | 700 | — | 700 |
| Change in unrealized loss on marketable securities | — | — | — | — | — | — | 1 | — | 1 |
| Issuance of Series A Convertible Preferred Stock | 40,949,999 | 40,622 | — | — | — | — | (108) | — | (108) |
| Settlement of Series A investor instrument | — | 328 | — | — | — | — | 1,863 | — | 1,863 |
| Exchange of common stock held by LLC entity for Series A-1 Junior Preferred Stock | — | — | (8,578,661) | (8) | 78,666,209 | 79 | (71) | — | — |
| Net loss | — | — | — | — | — | — | — | (23,178) | (23,178) |
| Balance at September 30, 2017(unaudited) | 80,949,999 | $ 80,950 | 1,770,302 | $ 2 | 78,666,209 | $ 79 | $ 47,784 | $ (99,721) | $ (51,856) |

The accompanying notes are an integral part of these financial statements

**Rhythm Pharmaceuticals, Inc.**

**Condensed Statements of Cash Flows**

**(in thousands, except share and per share data)**

**(Unaudited)**

| | Nine Months Ended September 30, | |
|---|---|---|
| | 2017 | 2016 |
| **Operating activities** | | |
| Net loss | $ (23,178) | $ (17,506) |
| Adjustments to reconcile net loss to cash used in operating activities: | | |
| Stock-based compensation expense | 1,569 | 859 |
| Depreciation and amortization | 163 | 89 |
| Non-cash rent expense | (56) | 29 |
| Mark to market revaluation of Series A Investor Instrument | 1,863 | — |
| Changes in operating assets and liabilities: | | |
| Prepaid expenses and other current assets | (972) | (272) |
| Deferred issuance costs | (1,689) | (348) |
| Tenant improvement allowance | — | 376 |
| Accounts payable, accrued expenses and other current liabilities | 830 | (335) |
| Deferred grant income | — | (71) |
| Due to related parties | (105) | 139 |
| Net cash used in operating activities | (21,575) | (17,040) |
| **Investing activities** | | |
| Purchases of short-term investments | (13,021) | (11,211) |
| Maturities of short-term investments | 14,506 | 7,054 |
| Purchases of property, plant and equipment | (78) | (1,057) |
| Net cash provided by (used in) investing activities | 1,407 | (5,214) |
| **Financing activities** | | |
| Net proceeds from issuance of Series A Convertible Preferred Stock | 40,842 | — |
| Proceeds from the exercise of stock options | 700 | — |
| Net cash provided by financing activities | 41,542 | — |
| Net increase (decrease) in cash and cash equivalents | 21,374 | (22,254) |
| Cash and cash equivalents at beginning of period | 6,540 | 34,869 |
| Cash and cash equivalents at end of period | $ 27,914 | $ 12,615 |

The accompanying notes are an integral part of these financial statements

**Rhythm Pharmaceuticals, Inc.**

**Notes to Unaudited Condensed 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 peptide therapeutics for the treatment of genetic deficiencies that result in life-threatening metabolic disorders. The Company's lead product candidate is setmelanotide (RM-493), which is a potent, first-in-class, melanocortin-4 receptor, or MC4R, agonist for the treatment of rare genetic disorders of obesity caused by MC4 pathway deficiencies. The Company is currently evaluating setmelanotide for the treatment of six genetic disorders of obesity: pro-opiomelanocortin, or POMC, leptin receptor, or LepR, Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous, and POMC epigenetic disorders.

***Corporate Reorganization***

The Company is a Delaware corporation organized in February 2013 under the name Rhythm Metabolic, Inc. Prior to the Company's organization and the Corporate Reorganization referred to below, the Company was part of Rhythm Pharmaceuticals, Inc. (the "Predecessor Company"), a Delaware corporation which was organized in November 2008 and which commenced active operations in 2010.

In March 2013, the Predecessor Company underwent a corporate reorganization, (the "Corporate Reorganization"), pursuant to which all of the outstanding equity securities of the Predecessor Company were exchanged for units of Rhythm Holding Company, LLC, a newly-organized limited liability company (the "LLC entity"). After the consummation of this exchange and as part of the Corporate Reorganization, the Predecessor Company contributed setmelanotide and the MC4R agonist program to the Company and distributed to the LLC entity all of the then issued and outstanding shares of the Company's stock. The result of the Corporate Reorganization was that the Company and the Predecessor Company became wholly-owned subsidiaries of the LLC entity and the two product candidates and related programs that were originally held by the Predecessor Company were separated, with relamorelin and the ghrelin agonist program being retained by the Predecessor Company and setmelanotide and the MC4R agonist program being held by the Company. The Predecessor Company, after consummation of the Corporate Reorganization, is referred to within these Notes to Financial Statements as the Relamorelin Company and/or Motus.

On October 13, 2015, the Relamorelin Company changed its name to Motus Therapeutics, Inc. ("Motus") and the Company changed its name to Rhythm Pharmaceuticals, Inc. On December 15, 2016, Motus was sold to a large pharmaceutical company. On August 21, 2017, the LLC entity distributed to its members all of its shares of the Company (see Note 6 for further discussion). Following this distribution, the LLC entity no longer owns any of the Company's shares.

***Liquidity***

The Company has incurred losses since inception and negative cash flows from operating activities. As of September 30, 2017, the Company had an accumulated deficit of $99,721. The Company anticipates that it will continue to incur significant operating losses for the next several years as it continues to develop setmelanotide. The Company had cash and short-term investments of $30,415 as of September 30, 2017. In addition, the Company received additional funding in connection with its initial public offering subsequent to quarter-end (see Note 10, "Subsequent Events"). The net proceeds from this offering were approximately $125.8 million after deducting underwriting discounts and commissions and offering expenses. 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 first half of 2019.

**2. Summary of Significant Accounting Policies**

***Basis of Presentation***

The Company's unaudited condensed 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, 2017, the statements of operations and comprehensive loss for the three and nine months ended September 30, 2017 and 2016, the statement of cash flows for the nine months ended September 30, 2017 and 2016, and the statement of convertible preferred stock and stockholders' equity (deficit) for the nine months ended September 30, 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, 2017 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 MC4R agonist programs were transferred to the Company as part of the Corporate Reorganization on March 21, 2013. These financial statements include the results of operations of setmelanotide and the MC4R agonist program from its inception. As part of the Corporate Reorganization, the Company also entered into a formal payroll services intercompany agreement with the Relamorelin Company. On November 16, 2016, the employees of the Relamorelin Company that were providing services to the Company, terminated their employment contracts with the Relamorelin Company and entered into new employment agreements with the Company. On December 15, 2016, the Relamorelin Company closed its sale to a large pharmaceutical company. At September 30, 2017, the Company had seventeen employees directly employed by the Company. During 2016, costs have been allocated to the Company for the purposes of preparing the financial statements based on a specific identification basis or, when specific identification is not practicable, a proportional cost allocation method which allocates expenses based upon the percentage of employee time and research and development effort expended on the Company's business as compared to total employee time and research and development effort of the combined Motus and Rhythm. The proportional use basis adopted to allocate shared costs is in accordance with the guidance of SEC Staff Accounting Bulletin (“SAB”) Topic 1B, *Allocation Of Expenses And Related Disclosure In Financial Statements Of Subsidiaries, Divisions Or Lesser Business Components Of Another Entity*. Management has determined that the method of allocating costs to the Company is reasonable. Cost allocation was no longer required subsequent to the 2016 sale of the Relamorelin Company.

Management believes that the statements of operations include a reasonable allocation of costs and expenses incurred by the Relamorelin Company, which benefited the Company. However, such amounts may not be indicative of the actual level of costs and expenses that would have been incurred by the Company if it had operated as an independent company or of the costs and expenses expected to be incurred in the future. Management has not presented an estimate of what the expenses of the Company would have been on a standalone basis as it was not practicable to make a reasonable estimate. As such, the financial information herein may not necessarily reflect the financial position, results of operations and cash flows of the Company expected in the future or what it would have been had it been an independent company during the periods presented.

As described above, Relamorelin Company employee costs are allocated to the Company based on a proportional use method. For those employees who became employees of the Company on November 16, 2016, their full employment cost was $2,727 for the year ended December 31, 2016.

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 September 29, 2017 the Company filed a third amended and restated certificate of incorporation with the Secretary of State of the State of Delaware to reflect the reverse stock split and authorize 29,919,979 of its shares of common stock, $0.001 par value per share and 159,616,209 shares of preferred stock, $0.001 par value per share.

***Use of Estimates***

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent liabilities at the date of the financial statements and the reported amounts of revenue and expenses during the reporting period. The Company bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes to be reasonable under the circumstances. This process may result in actual results differing materially from those estimated amounts used in the preparation of the financial statements if these results differ from historical experience, or other assumptions do not turn out to be substantially accurate, even if such assumptions are reasonable when made. Significant estimates relied upon in preparing these financial statements include the allocation of costs from the Relamorelin Company in accordance with SAB Topic 1B, accrued expenses, stock-based compensation expense, the valuation allowance on the Company's deferred tax assets, and the fair value of the Series A Investor Instrument (see Note 4).

***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 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. 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 consideration the most recent sale of our convertible preferred stock and the investors' right to invest in a subsequent

tranche. As the Company is a private company and lacks company-specific historical and implied volatility information of our 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 Options. The risk-free interest rate was determined by reference to the U.S. Treasury yield curve for time periods approximately equal to the estimated term of the Series A Investor Call Option. A dividend yield of zero was assumed.

***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 to 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 is 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.

Basic and diluted earnings per share is calculated as follows:

| | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | 2017 | 2016 | 2017 | 2016 |
| Numerator: | | | | |
| Net loss | $ (10,016) | $ (6,391) | $ (23,178) | $ (17,506) |
| Cumulative dividends on convertible preferred shares | (1,413) | (800) | (3,785) | (2,396) |
| Loss attributable to common shares—basic and diluted | $ (11,429) | $ (7,191) | $ (26,963) | $ (19,902) |
| Denominator: | | | | |
| Weighted-average number of common shares—basic and diluted | 6,404,254 | 10,196,292 | 8,918,389 | 10,196,292 |
| Loss per common share—basic and diluted | $ (1.78) | $ (0.71) | $ (3.02) | $ (1.95) |

**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 2016-02 on its financial position and results of operations.

In March 2016, the FASB issued ASU 2016-09, *Improvements to Employee Share-Based Payment Accounting (Topic 718)* that changes the accounting for certain aspects of share-based payments to employees. The guidance requires the recognition of the income tax effects of awards in the income statement when the awards vest or are settled, thus eliminating additional paid in capital pools. The guidance also allows for the employer to repurchase more of an employee's shares for tax withholding purposes without triggering liability accounting. In addition, the guidance allows for a policy election to account for forfeitures as they occur rather than on an estimated basis. The guidance is effective for annual periods beginning after December 15, 2016, and interim periods within those annual periods with early adoption permitted. Accordingly, the standard is effective for the Company on January 1, 2018. The Company adopted the standard as of January 1, 2017. The adoption did not have a material impact on the Company's financial position, results of operations or cash flows.

In November 2016, the FASB issued ASU 2016-18, Statement of Cash Flows (Topic 230): Restricted Cash 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 the standard as of January 1, 2017. The adoption did not have a material impact on the Company’s statements of cash flows.

In May 2017, the FASB issued ASU 2017-09, Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting. ASU 2017-09 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. ASU 2017-09 is effective for fiscal years, and interim periods within those years, beginning after December 15, 2017. The adoption of ASU 2017-09 is not expected to have a material impact on the Company's financial position or results of operations.

In July 2017, the FASB issued ASU 2017-11, Earnings Per Share (Topic 260), Distinguishing Liabilities from Equity (Topic 480) and Derivatives and Hedging (Topic 815): I. Accounting for Certain Financial Instruments with Down Round Features; II. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception. Part I of this update addresses the complexity of accounting for certain financial instruments with down round features. Down round features are features of certain equity-linked instruments (or embedded features) that result in the strike price being reduced on the basis of the pricing of future equity offerings. Current accounting guidance creates cost and complexity for entities that issue financial instruments (such as warrants and convertible instruments) with down round features that require fair value measurement of the entire instrument or conversion option. Part II of this update addresses the difficulty of navigating Topic 480, Distinguishing Liabilities from Equity, because of the existence of extensive pending content in the FASB Accounting Standards Codification. This pending content is the result of the indefinite deferral of accounting requirements about mandatorily redeemable financial instruments of certain nonpublic entities and certain mandatorily redeemable noncontrolling interests. The amendments in Part II of this update do not have an accounting effect. ASU 2017-11 is effective for fiscal years, and interim periods within those years, beginning after December 15, 2018. The Company is currently assessing the potential impact of adopting ASU 2017-11 on its financial statements and related disclosures.

**3. Accrued Expenses**

Accrued expenses consisted of the following:

| | September 30, 2017 | December 31, 2016 |
|---|---|---|
| Research and development costs | $ 2,005 | $ 2,049 |
| Professional fees | 371 | 182 |
| Payroll related | 625 | 344 |
| Other | 107 | 80 |
| Accrued expenses | $ 3,108 | $ 2,655 |

**4. Preferred Stock**

In January 2017, pursuant to the Series A preferred stock purchase agreement, by and among the Company and certain purchasers, and as part of an initial tranche closing, the Company issued 20,475,001 shares of Series A convertible preferred stock, par value $0.001 per share, at a purchase price of $1.00 per share, resulting in net proceeds of $20,377 to the Company (the “January 2017 Initial Tranche Closing”). The Series A preferred stock purchase agreement provided for the delayed issuance by the Company of up to an additional 20,474,998 shares of Series A convertible preferred stock as part of a second tranche closing at a purchase price of $1.00 per share (the “2017 Series A Investor Right/Obligation”). The second tranche is contingent upon: (1) the Company's cash, cash equivalents and short-term investments balance, net of accounts payable and accrued liabilities, falling below $5.0 million and (2) the Company's satisfaction of contractual and customary representations and warranties. Unless otherwise mutually agreed upon in writing, the rights and obligations underlying the second tranche (if not previously executed) will terminate on the first to occur of the following dates: (1) the date (the “Roadshow Acceleration Date”) on which the Company files with the U.S. Securities and Exchange Commission, or SEC, the last pre-effective amendment to the registration statement prior to the start of the Company's roadshow in connection with the Intial Public Offering, or IPO, provided, that such termination shall be contingent upon the consummation of the IPO pursuant to the same registration statement that was on file with the SEC on the Roadshow Acceleration Date, without withdrawal thereof or filing of a subsequent registration statement in replacement thereof; and (2) the date of the consummation of a Deemed Liquidation Event (as defined below). To the extent the closing of the second tranche has not already taken place, the investors in the first tranche also have a call right on the shares underlying the second tranche whereby such shares can be purchased for the same price as the second tranche (the “2017 Series A Investor Call Option”). The 2017 Series A Investor Call Option terminates upon the Roadshow Acceleration Date. The 2017 Series A Investor Right/Obligation and the 2017 Series A Investor Call Option have been evaluated and determined to be a free standing instrument, the 2017 Series A Investor Instrument. The 2017 Series A Investor Instrument is being accounted for as a liability (see Note 2).

In August 2017, the Series A Investors waived the $5.0 million cash balance requirement of the Series A Investor Right/Obligation and closed the second tranche of the series A preferred stock financing. The Company issued 20,474,998 shares of Series A convertible preferred stock, par value $0.001 per share, at a purchase price of $1.00 per share, resulting in gross proceeds of $20,475 to the Company. The 2017 Series A Investor Call Option expired unexercised at that time.

Upon the closing of an initial public offering with a minimum price per share and gross proceeds of at least $1.00 and $50.0 million, respectively, the Series A convertible preferred stock will automatically convert into shares of common stock on a 9.17-for-1 basis.

The holders of the Series A convertible preferred stock have the following rights and preferences:

***Voting Rights***

The holders of Series A convertible preferred stock are entitled to vote, together with the holders of common stock, on all matters submitted to stockholders for a vote. Each preferred stockholder is entitled to the number of votes equal to the number of shares of common stock into which each preferred share is convertible at the time of such vote. In addition, pursuant to the Company's charter, the holders of record of the outstanding shares of Series A convertible

preferred stock are entitled to elect one director to serve as the Series A preferred director on the board of directors of the Company.

***Dividends***

The holders of Series A convertible preferred stock are entitled to receive dividends in preference to any dividend on common stock at the rate of 8.0% per year of the original issue price. Dividends shall accrue annually, whether or not declared, and shall be cumulative. The Company may not declare, pay or set aside any dividends on shares of any other class or series of capital stock of the Company unless the holders of Series A convertible preferred stock then outstanding shall first receive, or simultaneously receive, dividends on each outstanding share of Series A convertible preferred stock. Through September 30, 2017 and December 31, 2016, no dividends had been declared or paid by the Company. Accrued dividends, whether or not declared, shall also be payable upon any liquidation event. At September 30, 2017 and December 31, 2016, cumulative preference dividends amounted to $7,914, or $0.10 per share and $4,129, or $0.10 per share, respectively.

***Liquidation***

In the event of any liquidation, dissolution or winding-up of the Company or a Deemed Liquidation Event (as defined below), the holders of Series A convertible preferred stock then outstanding shall be entitled to be paid out of the assets of the Company available for distribution to stockholders, and before any payment shall be made to holders of common stock, an amount per share equal to greater of (i) the original issue price per share, plus any accrued but unpaid dividends thereon, whether or not declared, plus any declared but unpaid dividends thereon, if any, or (ii) such amount per share as would have been payable had all shares of Series A convertible preferred stock been converted to common stock prior to such liquidation. If upon such event, the assets of the Company available for distribution are insufficient to permit payment in full to the holders of Series A convertible preferred stock, the proceeds will be ratably distributed among the holders of Series A convertible preferred stock in proportion to the respective amounts that they would have received if they were paid in full. After payments have been made in full to the holders of Series A convertible preferred stock, the remaining assets of the Company available for distribution will be distributed among the holders of Series A convertible preferred stock, the holders of the Series A-1 convertible junior preferred stock, and the holders of common stock as if the shares of Series A convertible preferred stock and Series A-1 convertible junior preferred stock were converted to common stock immediately prior to the liquidation event.

A merger, acquisition, sale of voting control or other transaction of the Company in which the stockholders of the Company do not own a majority of the outstanding shares of the surviving company shall be considered a Deemed Liquidation Event. A sale, exclusive license, transfer or other disposition of all or substantially all of the assets of the Company shall also be considered a Deemed Liquidation Event. Each share of Series A convertible preferred stock may be redeemed at the option of the holder upon the occurrence of a deemed liquidation event. As of September 30, 2017 and December 31, 2016, the liquidation preference of the outstanding shares of Series A convertible preferred stock was approximately $88,864 and $44,129, respectively.

***Conversion***

Each share of Series A convertible preferred stock is convertible into common stock at the option of the stockholder at any time after the date of issuance. In addition, each share of Series A convertible preferred stock will be automatically converted into shares of common stock, at the applicable conversion ratio then in effect, upon the earlier of (i) a qualified public offering with gross proceeds of at least $50,000 and a price of not less than $1.00 per share, subject to appropriate adjustment for any stock dividend, stock split, combination or other similar recapitalization, and (ii) the date specified by vote or written consent of the holders of at least two-thirds of the then outstanding shares of series A preferred stock. The shares of Series A convertible preferred stock will be converted to common stock, at par value, with the remainder recorded to additional paid-in capital.

The conversion ratio of the Series A convertible preferred stock is determined by dividing the original issue price per share by the conversion price of $9.17 per share, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or recapitalization affecting the Series A convertible preferred stock. As of September 30, 2017

and December 31, 2016, the outstanding shares of Series A convertible preferred stock were convertible into 8,827,692 and 4,362,050 shares of common stock, respectively.

**5. Fair Value of Financial Assets and Liability**

As of September 30, 2017 and December 31, 2016, the carrying amount of cash and cash equivalents and short-term investments was $30,415 and $10,537, 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 $28,722 and $7,984 as of September 30, 2017 and December 31, 2016, respectively.

A financial liability was recognized by the Company during the nine months ending September 30, 2017 related to the 2017 Series A Investor Instrument that was exercised in August 2017. The liability was valued based on significant inputs not observable in the market, which represents a Level 3 measurement within the fair value hierarchy. For the year ended December 31, 2016, the Company had no financial liabilities outstanding measured at fair value.

The following tables present information about the Company's financial assets and liabilities measured at fair value on a recurring basis and indicate the level of the fair value hierarchy utilized to determine such fair values:

| | Fair value Measurements as of September 30, 2017 using: | | | |
|---|---|---|---|---|
| | Level 1 | Level 2 | Level 3 | Total |
| Assets: | | | | |
| Cash Equivalents: | | | | |
| Government Funds | $ — | $ — | $ — | $ — |
| Money Market Funds | 26,221 | — | — | 26,221 |
| Marketable Securities: | | | | |
| Government Funds | 2,501 | — | — | 2,501 |
| Total | $ 28,722 | $ — | $ — | $ 28,722 |
| Liabilities: | | | | |
| 2017 Series A Investor Instrument | $ — | $ — | $ — | $ — |
| Total | $ — | $ — | $ — | $ — |

| | Fair value Measurements as of December 31, 2016 using: | | | |
|---|---|---|---|---|
| | Level 1 | Level 2 | Level 3 | Total |
| Assets: | | | | |
| Cash Equivalents: | | | | |
| Government Funds | $ 2,000 | $ — | $ — | $ 2,000 |
| Money Market Funds | 1,987 | — | — | 1,987 |
| Marketable Securities: | | | | |
| Government Funds | 3,997 | — | — | 3,997 |
| Total | $ 7,984 | $ — | $ — | $ 7,984 |

**Marketable Securities**

The following tables summarize the Company's marketable securities:

| | September 30, 2017 | | | |
|---|---|---|---|---|
| | Amortized Cost | Gross Unrealized Gains | Gross Unrealized Losses | Fair Value |
| Assets | | | | |
| Government Funds (due within 1 year) | $ 2,502 | $ — | $ (1) | $ 2,501 |
| | $ 2,502 | $ — | $ (1) | $ 2,501 |

| | December 31, 2016 | | | |
|---|---|---|---|---|
| | Amortized Cost | Gross Unrealized Gains | Gross Unrealized Losses | Fair Value |
| Assets | | | | |
| Government Funds (due within 1 year) | $ 3,997 | $ — | $ — | $ 3,997 |
| | $ 3,997 | $ — | $ — | $ 3,997 |

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 through the date of settlement | 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.

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.

**6. Common Stock**

In March 2013, the Company issued 10,196,292 shares of common stock at a purchase price of $0.001 per share. As of December 31, 2016, 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 will convert to common stock on a 9.17-to-1 basis upon the earlier of (i) a qualified public offering with gross proceeds of at least $50,000 and a price of not less than $1.00 per share, subject to appropriate adjustment for any stock dividend, stock split, combination or other similar recapitalization, and (ii) the date specified by vote or written consent of the holders of the requisite holders of series A preferred stock and series A-1 junior preferred stock.

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.

**7. 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 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.

In January 2016, the Company entered into a licensing agreement with Camurus AB, or Camurus, for the use of Camurus’ drug delivery technology. The contract includes a non-refundable and non-creditable signing fee of $500, which was paid during January 2016. The Camurus Agreement also includes up to $7,750 in one-time, non-refundable development milestones achievable upon certain regulatory successes. The Company is also required to pay to Camurus royalties, mid to mid-high single digit, on a product-by-product and country-by-country basis of annual net sales, until the later of (i) 10 years after the date of first commercial sale of such product in such country; or (ii) the expiration of the last to expire valid claim of all licensed patent rights in such country covering such product. The Company is also required to pay one-time, non-refundable, non-creditable sales milestones upon the achievement of certain sales levels for such product and cannot be in excess of $57,000.

In March 2017, the Company achieved the first milestone event associated with this license agreement. The Company completed the first manufactured batch using the Camurus drug delivery technology and filed an investigational new drug application with the FDA. The fee associated with this milestone was $250.

**8. Related-Party Transactions**

The Company shared costs with the Relamorelin Company, its affiliate, including payroll, facilities, information technology and other research and development and general and administrative overhead costs. Additionally, the Relamorelin Company had paid certain Company expenses directly on behalf of the Company. Shared costs incurred by the Relamorelin Company and Company expenses paid by the Relamorelin Company on behalf of the Company are allocated from the Relamorelin Company to the Company as described in Note 1 and Note 2. The Relamorelin Company was sold to a large pharmaceutical company on December 15, 2016.

The LLC entity made payments on behalf of the Company totaling $105 related to allocated 2016 employee bonuses. Those costs are recorded as a payable due to the LLC entity from the Company at December 31, 2016 on the balance sheet.

Expenses paid directly by the Company to consultants considered to be related parties amounted to $294, $880, $184 and $386 for the three and nine months ended September 30, 2017 and 2016, respectively. Outstanding payments due to these related parties as of September 30, 2017 and December 31, 2016 were $130 and $50, respectively, and were included within accounts payable on the balance sheet. Expenses paid by the Relamorelin Company to these related parties amounted to zero, zero, $173 and $622 for the three and nine months ended September 30, 2017 and 2016, respectively.

Employees of certain holders of series A and series B convertible preferred units of the LLC entity, have been retained as consultants supporting development activities of the Company and the Relamorelin Company for which the holders are paid cash compensation pursuant to consulting arrangements. Compensation payments related to these consultants totaled $33, $77, $11 and $48 for the three and nine months ended September 30, 2017 and 2016, respectively.

**9. Income Taxes**

In the Company's financial statements, income taxes, including deferred tax balances, have been calculated on a separate tax return basis. Certain of the Company's activities and costs have been included in the tax returns filed by the Relamorelin Company and the LLC entity. Prior to the Corporate Reorganization, the Company's operations were included in the tax returns filed by the Predecessor Company. The Company has filed tax returns on its own behalf since the Corporate Reorganization.

For the year ended December 31, 2016, the Company did not have a current or deferred income tax expense or benefit as the entity has incurred losses since inception and has provided a full valuation allowance against its deferred tax assets.

**10. Subsequent Events**

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 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 $125,780 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. After the IPO, our outstanding common shares were 27,284,140. The financial statements as of September 30, 2017, including share and per share amounts, do not include the effects of the IPO.

On October 10, 2017 upon consummation of the Company’s IPO, the Company adopted the 2017 equity incentive plan (the “2017 plan”). The 2017 plan serves as the successor to the 2015 equity incentive plan (the “2015 plan”), and no further awards will be made under the 2015 plan. All awards outstanding under the 2015 plan have been treated as outstanding under the 2017 plan. The aggregate number of shares of the Company’s common stock which may be issued

under the 2017 plan or with respect to which awards may be granted may not exceed 4,018,538 shares. The number of shares which may be issued under the 2017 plan includes shares of common stock available for issuance under the 2015 plan, including the portion of those shares subject to options outstanding on that date. The number of shares authorized under the 2017 plan will be increased each January 1, by an amount equal to 4% of the Company's outstanding shares of stock as of the end of the immediately preceding fiscal year.

**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 financial statements and the related notes and other financial information included elsewhere in this Quarterly Report on Form 10-Q and with our audited financial statements and the notes thereto for the year ended December 31, 2016 included in our prospectus dated October 4, 2017 filed with the Securities and Exchange Commission pursuant to Rule 424(b) under the Securities Act of 1933, as amended. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report on Form 10-Q, including statements regarding our financial performance, including our expectations regarding our existing cash, operating losses, expenses and sources of future financing; statements regarding our plans to research, develop and commercialize setmelanotide, if approved; statements regarding the impact of changes in accounting standards; statements regarding our ability to hire and retain necessary personnel; statements regarding our ability to protect our intellectual property; statements regarding our ability to negotiate our collaboration agreements, if needed, 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 could differ materially from the results described in or implied by such forward-looking statements. Forward-looking statements speak only as of the date hereof, and, except as required by law, we undertake no obligation to update or revise these forward-looking statements.*

**Overview**

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

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

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 seventeen employees, five of whom hold Ph.D. or M.D. degrees. Of these employees, twelve are engaged in development and commercialization activities and five are engaged in support administration, including business development and finance. In the near-term, we expect to significantly expand our clinical, commercial and finance personnel, in particular, and will incur increased expenses as a result.

Our operations to date have been limited primarily to conducting research and development activities for setmelanotide. To date, we have not generated any product revenue and have financed our operations primarily through capital contributions from the Predecessor Company, the Relamorelin Company and the LLC entity and, more recently, the private placement of equity securities to outside investors. On October 10, 2017 we completed our intial 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, the Company's outstanding shares of convertible preferred stock were automatically converted into 17,406,338 shares of common stock. The financial statements as of September 30, 2017, including share and per share amounts, do not include the effects of the IPO. 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, 2017, we had an accumulated deficit of $99.7 million. Our net losses were $10.0 million, $23.2 million, $6.4 million and $17.5 million for the three and nine months ended September 30, 2017 and 2016, 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, 2017, our existing cash and cash equivalents and short-term investments were approximately $30.4 million and after giving effect to the aggregate net proceeds from our IPO in October 2017, $156.2 million. We expect that the net proceeds of this offering will enable us to fund our operating expenses into the first half of 2019.

***Corporate Background and Distribution***

We are a Delaware corporation organized in February 2013 under the name Rhythm Metabolic, Inc., and as of October 2015, under the name Rhythm Pharmaceuticals, Inc. Prior to our organization and the Corporate Reorganization 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 August 2015, December 2015, January 2017 and August 2017, we sold 25,000,000 shares, 15,000,000 shares, 20,475,001 shares and 20,474,998 shares, respectively, of our series A 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.

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

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

**Financial Operations Overview**

***Revenue***

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

***Research and development expenses***

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

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

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

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

| | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| **Research and Development Summary** | **2017** | **2016** | **2017** | **2016** |
| | (in thousands) | | | |
| Setmelanotide Program | $ 5,971 | $ 5,419 | $ 16,241 | $ 13,963 |

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

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

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

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

***General and administrative expenses***

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

The following table summarizes our current general and administrative expenses.

| | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | 2017 | 2016 | 2017 | 2016 |
| | (in thousands) | | | |
| General and administrative expense | $ 2,315 | $ 982 | $ 5,188 | $ 3,567 |

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

***Basis of Presentation***

***Presentation***

We have historically existed and functioned as part of the consolidated businesses of the Predecessor Company. Our MC4 business was contributed to us from the Predecessor Company on March 21, 2013 as part of the Corporate Reorganization. At that time, we also entered into the Payroll Services Agreement. In December 2016, the shared employees terminated their existing employment agreements and entered into new agreements with us. Until December 2016, we shared costs with the Relamorelin Company, including finance, accounting, research and development and operations. These shared costs were allocated to us from the Relamorelin Company for the purposes of preparing the financial statements based on a specific identification basis or, when specific identification is not practicable, a proportional cost allocation method which allocates expenses based upon the percentage of employee time and research and development effort expended on our business as compared to total employee time and research and development effort. The proportional use basis adopted to allocate shared costs is in accordance with the guidance of Staff Accounting Bulletin Topic 1B. Our management has determined that the proportional use method of allocating costs to us from the Relamorelin Company is reasonable.

***Accrued research and development expenses***

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

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

***2017 Series A Investor Instrument***

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. 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. 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 Options, risk-free interest rate, expected dividend yield and expected volatility of the price of the underlying preferred stock. We determined the fair value per share of the underlying preferred stock by taking into consideration the most recent sale of our convertible preferred stock and the investors' right to invest in a subsequent tranche. As we are a private company and lack company-specific historical and implied volatility information of our stock, we estimated our expected stock volatility based on the historical volatility of publicly traded peer companies for a term comparable to the estimated term of the 2017 Series A Investor Call Options. The risk-free interest rate was determined by reference to the U.S. Treasury yield curve for time periods approximately equal to the estimated term of the 2017 Series A Investor Call Options. A dividend yield of zero was assumed.

***Stock-based compensation***

Prior to August 2015, we did not have our own equity compensation plan. In August 2015, our Board of Directors and our stockholders approved and we adopted the 2015 equity incentive plan, as amended and in effect prior to the closing of 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 4,018,538 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 2015 Plan provides that the exercise price of incentive stock options cannot be less than 100% of the fair market value of the common stock on the date of the award for participants who own less than 10% of the total combined voting power of stock, and not less than 110% for participants who own more than 10% of the voting power. Options and restricted stock granted under the 2015 Plan will vest over periods as determined by our Compensation Committee and approved by our Board of Directors.

We estimate the fair value of our stock-based awards to employees and non-employees using the Black-Scholes option-pricing model, which requires the input of highly subjective assumptions, including (a) the expected volatility of our stock, (b) the expected term of the award, (c) the risk-free interest rate, and (d) expected dividends. Due to the lack of a public market for the trading of our common stock and a lack of company-specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of companies in the pharmaceutical and biotechnology 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, 2016, we do not have any uncertain tax positions.

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

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

Utilization of the net operating loss and tax credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that have occurred previously or that could occur in the future, as provided by Section 382 of the 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 three months ended September 30, 2017 and 2016***

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

| | Three Months Ended September 30, | | Change | |
|---|---|---|---|---|
| | 2017 | 2016 | $ | % |
| | (in thousands) | | | |
| **Statement of Operations Data:** | | | | |
| Operating Expenses: | | | | |
| Research and development | $ 5,971 | $ 5,419 | $ 552 | 10 % |
| General and administrative | 2,315 | 982 | 1,333 | 136 % |
| Total operating expenses | 8,286 | 6,401 | 1,885 | 29 % |
| Loss from operations | (8,286) | (6,401) | (1,885) | 29 % |
| Other (expense) income, net | (1,730) | 10 | (1,740) | NM % |
| Net loss and comprehensive loss | $ (10,016) | $ (6,391) | $ (3,625) | 57 % |

*Research and development expense.* Research and development expense increased by $0.6 million to $6.0 million in 2017 from $5.4 million in 2016, an increase of 10%. The increase was primarily due to the initiation of additional new clinical trials in 2017 and an increase in other development activities associated with setmelanotide, offset by the completion of some pre-clinical research studies. We hired additional personnel in the clinical and development departments during the quarter ended September 30, 2017.

*General and administrative expense.* General and administrative expense increased by $1.3 million to $2.3 million in 2017 from $1.0 million in 2016, an increase of 136%. The increase was primarily due to stock compensation expense related to the revaluation of certain option grants to our former president upon changing from an employee to nonemployee status, the legal costs related to the distribution of the LLC entity’s common shares to its members and general office expenses due to the increase in headcount during the quarter ended September 30, 2017.

***Comparison of nine months ended September 30, 2017 and 2016.***

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

| | Nine Months Ended September 30, | | Change | |
|---|---|---|---|---|
| | 2017 | 2016 | $ | % |
| | (in thousands) | | | |
| **Statement of Operations Data:** | | | | |
| Operating Expenses: | | | | |
| Research and development | $ 16,241 | $ 13,963 | $ 2,278 | 16 % |
| General and administrative | 5,188 | 3,567 | 1,621 | 45 % |
| Total operating expenses | 21,429 | 17,530 | 3,899 | 22 % |
| Loss from operations | (21,429) | (17,530) | (3,899) | 22 % |
| Other income (loss) | (1,749) | 24 | (1,773) | NM % |
| Net loss and comprehensive loss | $ (23,178) | $ (17,506) | $ (5,672) | 32 % |

*Research and development expense.* Research and development expense increased by $2.3 to $16.2 million in 2017 from $14.0 million in 2016, an increase of 16%. The increase was primarily due to the initiation of additional new clinical trials in 2017 and an increase in other market development activities associated with setmelanotide. We hired additional personnel in the clinical operations department at the end of 2016 and throughout 2017.

*General and administrative expense.* General and administrative expense increased by $1.6 million to $5.2 million in 2017 from $3.6 million in 2016, an increase of 45%. The increase was primarily due to stock compensation expense related to new option grants in 2017, legal costs related to the distribution of the LLC entity's common shares to its members and general office expenses due to the increase in headcount at the end of 2016 and throughout 2017.

**Liquidity and Capital Resources**

As of September 30, 2017, our existing cash and cash equivalents and short-term investments were approximately $30.4 million. After giving effect to the aggregate net proceeds of our IPO in October 2017 of $125.8 million, our cash and cash equivalents and short-term investments are $156.2 million as of September 30, 2017.

***Cash flows***

The following table provides information regarding our cash flows for the nine months ended September 30, 2017 and 2016:

| | Nine Months Ended September 30, | | |
|---|---|---|---|
| | 2017 | 2016 | Change |
| | (in thousands) | | |
| Net cash provided by (used in): | | | |
| Operating activities | $ (21,575) | $ (17,040) | $ (4,535) |
| Investing activities | 1,407 | (5,214) | 6,621 |
| Financing activities | 41,542 | — | 41,542 |
| Net increase (decrease) in cash and cash equivalents | $ 21,374 | (22,254) | 43,628 |

***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 $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 and deferred rent expense and the mark to market revaluation of the Series A Investor Instrument. The change in operating assets and liabilities reflected a total use of cash of approximately $1.9 million mainly for deferred issuance costs and prepaid expenses.

Net cash used in operating activities was $17.0 million for the nine months ended September 30, 2016, and consisted primarily of a net loss of $16.5 million adjusted for non-cash items, which consisted of stock-based compensation, depreciation and amortization and deferred rent expense. The significant items in the change in operating assets and liabilities include a decrease in accrued expenses of $0.3 million and an increase in deferred issuance costs of approximately $0.3 million.

***Net cash provided by (used in) investing activities***

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 used in investing activities for the nine months ended September 30, 2016 relates to the net purchases of short-term investments of $4.2 million and the buildout of our new headquarters facility and furniture and equipment of $1.0 million.

***Net cash provided by financing activities***

Net cash provided by financing activities was $41.5 million for the nine months ended September 30, 2017, and 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 expect to incur additional costs associated with operating as an independent company, and upon the closing of our IPO and operating as a public company.

We expect that the net proceeds from our IPO, together with our existing cash and cash equivalents, will enable us to fund our operating expenses at least through 2018. We may need to obtain substantial additional funding in connection with our research and development activities and any continuing operations thereafter. If we are unable to raise capital when needed or on favorable terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

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

- the scope, progress, results and costs of clinical trials for our setmelanotide program;
- the costs, timing and outcome of regulatory review of our setmelanotide program;
- the obligations owed to Ipsen Pharma S.A.S., or Ipsen, pursuant to our license agreement;
- the extent to which we acquire or in-license other product candidates and technologies;

- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims; and

- our ability to establish and maintain additional collaborations on favorable terms, if at all.

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

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

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

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

***Contractual obligations***

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

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

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

Future minimum payments under the operating lease agreements as of September 30, 2017, are as follows:

| | Operating Lease |
|---|---|
| 2017 | $ 73 |
| 2018 | 298 |
| 2019 | 305 |
| 2020 | 311 |
| 2021 | 131 |
| Total | 1,118 |

**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 in the ordinary course of our business. These risks primarily include interest rate sensitivities. As of September 30, 2017, we had cash, cash equivalents and short-term investments of approximately $30.4 million, and after giving effect to the aggregate net proceeds from our IPO in October 2017, approximately $156.2 million. The proceeds from our IPO were invested in United States treasury money market funds. The interest-earning instruments carry a degree of interest rate risk; however, historical fluctuations in interest income have not been significant. We are not exposed to 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.

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

**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, 2017, under the supervision of 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, 2017, 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 not presently known to us or that we currently deem immaterial also may impair our business operations. You should carefully consider the risks described below and the other information in this Quarterly Report on Form 10-Q, including our unaudited condensed 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.

Our net loss and comprehensive losses were $10.0 million, $23.2 million, $6.4 million and $17.5 million for the three months and the nine months ended September 30, 2017 and 2016, respectively. As of September 30, 2017, we had an accumulated deficit of $99.7 million. Substantially all of our operating losses have resulted from costs incurred in connection with our development program and from general and administrative costs associated with our operations. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' deficit and working capital. We expect our research and development expenses to significantly increase in connection with our additional clinical trials of setmelanotide and development of any other product candidates we may choose to pursue. In addition, if we obtain marketing approval for setmelanotide, we will incur significant sales, marketing and outsourced manufacturing expenses. 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;
- 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 the proceeds from our IPO primarily for the clinical development and regulatory approval of setmelanotide. Depending on the status of regulatory approval and, if approved, commercialization of setmelanotide, as well as the progress we make in the sale of setmelanotide, we may still require significant additional capital to fund the continued development of setmelanotide and our operating needs thereafter. We may also need to raise additional funds if we choose to pursue additional indications and/or geographies for setmelanotide or otherwise expand more rapidly than we presently anticipate.

Through August 2015, we received capital contributions from the Predecessor Company, the Relamorelin Company and the LLC entity. In August 2015, December 2015, January 2017 and August 2017, we raised aggregate gross proceeds of $25.0 million, $15.0 million, $20.5 million and $20.5 million, respectively, through our issuance of series A preferred stock. As of September 30, 2017, our cash and cash equivalents and short-term investments were approximately $30.4 million and after giving effect to the aggregate net proceeds from our IPO in October 2017, $156.2 million. We expect that the net proceeds from our IPO, together with our existing cash and cash equivalents, will be sufficient to fund our operating expenses into the first half of 2019. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements, or a combination of these approaches. We will also require additional capital to obtain regulatory approval for, and to commercialize, setmelanotide. Raising funds in the current economic environment may present additional challenges. Even if we believe 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 that planned for testing in our current pivotal Phase 3 clinical trials. The duration of effect of setmelanotide has only been studied in long-term durations for a small number of patients in our Phase 2 clinical trials and safety or efficacy issues may arise when more patients are studied in longer trials. It is possible that the effects seen in short-term clinical trials will not be replicated in long-term or larger clinical trials. In addition, not all of our trials demonstrated statistically significant weight loss and there can be no guarantee that future trials will do so.

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

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

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials after achieving positive results in early stage development, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, pre-clinical findings made while clinical trials were underway. We have completed the key toxicology studies that we believe the U.S. Food and Drug Administration, or the FDA, and the European Medicines Agency, or EMA, will require for approval, which include,

among others, chronic toxicity studies, reproductive and developmental toxicity studies, and juvenile toxicology studies. Based on the totality of animal testing results to date, including the lack of any observed genotoxicity or tissue proliferative activity of setmelanotide in chronic toxicity studies, we have requested that the FDA permit us to defer carcinogenicity studies until after approval of a new drug application, or NDA, for setmelanotide. Accordingly, we believe that we will be able to defer all carcinogenicity studies until after we receive regulatory approval to market setmelanotide. However, the FDA has indicated that it will not make a decision on our request until after reviewing our final toxicology study reports. Accordingly, at this time, there can be no guarantee that we will be able to achieve this deferral which could impact the timing of any potential NDA approval as well as the time frame to achieve commercialization.

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

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

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

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

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

- *POMC Deficiency Obesity.* There are approximately 50 patients with POMC deficiency obesity noted in a series of published case reports, each mostly reporting a single or small number of patients. However, we believe our addressable patient population for this deficiency may be approximately 100 to 500 patients in the United States, and a comparable addressable patient population in Europe, as most of the reported cases are from a small number of academic research centers, and because genetic testing for POMC deficiency is often unavailable and currently is rarely performed. Based on discussions with experts in rare diseases, we also believe the number of diagnosed cases could increase several-fold with increased awareness of this deficiency and the availability of new treatments.

- *LepR Deficiency Obesity and POMC Heterozygous Deficiency Obesity.* Our addressable patient population estimate for LepR deficiency obesity is approximately 500 to 2,000 patients in the United States, and for

POMC heterozygous deficiency obesity is approximately 4,000 patients in the United States, with a comparable addressable patient population for both indications in Europe. Our estimates are based on:

- epidemiology studies on LepR deficiency and POMC heterozygous deficiency in small cohorts of patients comprised of children with severe obesity and adults with severe obesity who have a history of early onset obesity;
- U.S. Census Bureau figures for adults and children, and Centers for Disease Control and Prevention, or CDC, prevalence numbers for severe adult obese patients (body mass index, or BMI, greater than 40 kg/ $m^2$) 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
  - We believe that with wider availability of genetic testing expected for Bardet-Biedl syndrome and increased awareness of new treatments, the number of patients diagnosed with this disorder will increase.
- *Alström Syndrome.* Our addressable patient population estimate for Alström syndrome is approximately 500 to 1,000 patients worldwide. This estimate is based on:
  - Published prevalence estimates of one in 1,000,000 in North America, which projects to approximately 325 people in the United States. We believe the majority of these patients are addressable patients; and
  - We believe that with wider availability of genetic testing expected for Alström syndrome and increased awareness of new treatments, the number of patients diagnosed with this disorder will increase.
- *POMC Epigenetic Disorders.* There is currently no epidemiology data that defines the prevalence of POMC epigenetic disorders.

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

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

Another method to estimate the size of these ultra-rare populations by genetic epidemiology is using newly available large genomic databases, containing full genome sequencing or exome sequencing. Ultra-rare orphan diseases are generally categorized as those that affect fewer than 20 patients per million. We have begun some substantial efforts

with a series of such databases and/or collaborators. Much of our preliminary work has been with a database of approximately 140,000 genomes, which is representative of the U.S. population. These efforts generally are based on the prevalence of heterozygous mutations, as true null mutations are ultra-rare, and then standard scientific methods such as the Hardy-Weinberg equilibrium calculations, are applied to estimate the prevalence in the U.S. population. These methods make assumptions that may not be sufficiently robust for ultra-rare genetic disorders, and have the inherent variability of estimates for rare events. In addition, the databases currently available only provide limited clinical data, such as, age, weight and BMI, that would be needed to associate genetic defects with severe obesity. However, until these data are confirmed in further genetic epidemiology efforts in additional databases, we must continue to base our patient population estimates on clinical epidemiological information.

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

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

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

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

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

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

Patient enrollment is also affected by other factors including:

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

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays, could require us to abandon one or more clinical trials altogether and could delay or prevent our receipt of necessary regulatory approvals. Enrollment delays in our clinical trials may result in increased development costs for setmelanotide, which would cause the value of our company to decline and limit our ability to obtain additional financing.

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

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

- the FDA or other equivalent competent authorities in foreign jurisdictions may deny permission to proceed with our planned Phase 3 clinical trials or any other clinical trials we may initiate, or may place a clinical trial on hold;
- delays in filing or receiving approvals or additional IND that may be required;
- negative results from our ongoing and planned preclinical studies, or the FDA or other equivalent competent authorities in foreign jurisdictions requiring additional preclinical studies;
- delays in commencing additional necessary preclinical studies, including carcinogenicity and juvenile toxicology studies;
- delays in reaching or failing to reach agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

- since many already diagnosed patients are at academic sites, delays in conducting clinical trials at academic sites due to the particular challenges and delays typically associated with those sites;
- inadequate quantity or quality of setmelanotide or other materials necessary to conduct clinical trials, including delays in the manufacturing of sufficient supply of finished drug product;
- difficulties obtaining Institutional Review Board, or IRB, and/or ethics committee approval to conduct a clinical trial at a prospective site or sites;
- challenges in recruiting and enrolling patients to participate in clinical trials, including the size and nature of the patient population, the proximity of patients to clinical trial sites, eligibility criteria for the clinical trial, the nature of the clinical trial protocol, the availability of approved effective treatments for the relevant disease and competition from other clinical trial programs for similar indications;
- severe or unexpected drug-related side effects experienced by patients in a clinical trial, including side effects previously identified in our completed clinical trials;
- delays in identifying and recruiting patients with any of the genetic causes of obesity in indications that we are targeting;
- disagreement by the FDA, other regulatory agencies or the equivalent competent authorities in foreign jurisdictions with our clinical trial designs, which may in turn cause delays in initiating our clinical trials, or may lead to rejection of our interpretation of data from clinical trials or to changes in the requirements for approval even after it has reviewed and commented on the design for our clinical trials;
- the requirement to have a placebo controlled study even though the FDA and EMA did not impose one for POMC deficiency obesity, as we cannot be certain that this will be true for other indications or that the FDA or EMA, an advisory committee or the equivalent competent authorities in foreign jurisdictions will not change its guidance, as it has done so in the past for other open control trials;
- uncertainty related to the length of placebo-controlled intervals in clinical trials;
- the need to perform non-inferiority trials, which can be larger, longer and more costly, if treatment is approved for similar indications;
- potential delays in the initiation of our clinical trials of LepR deficiency obesity due to the fact that we have not yet had discussions with the FDA regarding clinical trials for LepR deficiency obesity and, accordingly, do not know if the FDA will disagree with our clinical trial design;
- POMC heterozygous deficiency may have additional challenges, including that the FDA the EMA, or the equivalent competent authorities in foreign jurisdictions may require that we show that setmelanotide works better in these patients than in the genetically normal population; other challenges associated with these patients may include additional delays in initiating clinical trials for this indication due to uncertainty about the subset of these patients who will respond effectively to setmelanotide and the lack of discussion for this indication with the FDA;
- reports from preclinical or clinical testing of other weight loss therapies may raise safety or efficacy concerns; and
- difficulties retaining patients who have enrolled in a clinical trial but may be prone to withdraw due to rigors of the clinical trial, lack of efficacy, side-effects, personal issues or loss of interest.

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

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

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

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

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

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

their hunger, and from their family members or caregivers on the effect of setmelanotide on the patients' food seeking behavior.

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

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

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

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

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

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

The safety data we have disclosed to date represents our interpretation of the data at the time of disclosure and they are subject to our further review and analysis. The only serious adverse event possibly attributed to setmelanotide in

our clinical trials was one report of atypical chest pain seen in our Phase 2 clinical trial with once daily SC injection, although there was no evidence of any serious respiratory or cardiac cause on careful examination. Overall, there have been five other serious adverse events in the overall clinical development program in addition to the serious adverse event described above: two others during treatment on setmelanotide, left arm numbness and influenza immunization reaction and three during treatment with placebo, including biliary dyskinesia, severe groin strain and pelvic inflammatory disease. None of these serious adverse events was considered related to setmelanotide.

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

In addition, our interpretation of the safety data from our clinical trials is contingent upon the review and ultimate approval of the FDA, other regulatory authorities or other equivalent competent authorities in foreign jurisdictions. The FDA or other equivalent competent authorities in foreign jurisdictions may not agree with our methods of analysis or our interpretation of the results. In addition, the long-term effects of setmelanotide have only been tested in a limited number of patients.

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

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

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

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

The FDA may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, or the Orphan Drug Act, the FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition, which is defined under the Federal Food, Drug and Cosmetic Act, or FDCA, as having a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in

the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States.

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

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

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

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

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

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

Under the Food and Drug Administration Safety and Innovation Act, or FDASIA, the FDA is authorized to give certain products "breakthrough therapy designation." Breakthrough therapy product candidate is defined as a product candidate that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that such product candidate may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. The FDA will seek to ensure the sponsor of breakthrough therapy product candidate receives intensive guidance on an efficient drug development program, intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review

and a rolling review process whereby the FDA may consider reviewing portions of an NDA before the sponsor submits the complete application. Product candidates designated as breakthrough therapies by the FDA may be eligible for other expedited programs, such as priority review, if supported by clinical data.

Designation as breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe setmelanotide meets the criteria for designation as breakthrough therapy for other uses, the FDA may disagree. In any event, the receipt of breakthrough therapy designation for a product candidate, or acceptance for one or more of the FDA's other expedited programs, may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and does not guarantee ultimate approval by the FDA. Additionally, the FDA may later decide that the product candidate no longer meets the conditions for designation and may withdraw designation at any time or decide that the time period for FDA review or approval will not be shortened.

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

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

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

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

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

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

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

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

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

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

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

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

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

Although we have been granted orphan drug designation for setmelanotide in treating PWS, we are not moving directly towards a Phase 3 trial in PWS at this time, but instead will be assessing how to proceed in another Phase 2 trial. We do not know the probability that we will be able to proceed to Phase 3 and/or approval, even when these efforts are completed. In addition, the experience by others suggests that PWS patients are high risk for adverse experiences and hence clinical trials in that population are extremely challenging. It may be both difficult to determine if adverse effects in this population are due to the disease, setmelanotide or some combination of both. PWS is a complex multigenic disease, and the hypothesis that PWS is an upstream MC4 pathway disorder is supported primarily on the role of only one of those genes, MAGEL2, in animal models of obesity. Our results may support that PWS is not an upstream MC4 pathway disorder. Alternatively, other design factors may have influenced the outcome of this trial, and we will be reassessing in 2018 the possibility of future Phase 2 trials in PWS that address the following potential factors: duration of treatment,

younger age of population, improved setmelanotide pharmacokinetics, consideration of higher doses, and operational limitations of the completed Phase 2 trial. There can be no assurances that some of the factors that affected the results of the PWS trials will not also adversely impact the results of our trials for other indications.

**Risks Related to the Commercialization of Setmelanotide**

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

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

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

In the European Union, in particular, each EU member state can restrict the range of medicinal products for which its national health insurance system provides reimbursement and can control the prices of medicinal products for human use marketed in its territory. As a result, following receipt of marketing authorization in an EU member state, through any application route, an applicant is required to engage in pricing discussions and negotiations with the competent pricing authority in the individual EU member states. Some EU member states operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed upon. Other EU member states approve a specific price for the medicinal product or may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. The downward pressure on healthcare costs in general, particularly prescription drugs, has become more intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, we may face competition for 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 and Sweden. HTA is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. HTA generally focuses on the clinical efficacy and effectiveness, safety, cost, and cost-effectiveness of individual medicinal products as well as their potential implications for the healthcare system. Those elements of medicinal products are compared with other treatment options available on the market. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU member states. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product varies between EU member states. In addition, pursuant to Directive 2011/24/EU on the application of patients' rights in cross-border healthcare, a voluntary network of national authorities or bodies responsible for HTA in the individual EU member states was established. The purpose of the network is to facilitate and support the exchange of scientific information concerning HTAs. This may lead to harmonization of the criteria taken into account in the conduct of HTAs between EU member states and in pricing and reimbursement decisions and may negatively affect price in at least some EU member states.

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

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

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

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

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

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

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

- the ability of setmelanotide to treat obesity caused by certain genetic deficiencies affecting the MC4 pathway and, if required by any competent authority in connection with the approval for these indications, to provide patients with incremental health benefits, as compared with other available treatments, therapies, devices or surgeries;

- the relative convenience and ease of SC injections as the necessary method of administration of setmelanotide, including as compared with other treatments for obese patients;

- the prevalence and severity of any adverse side effects associated with setmelanotide;

- limitations or warnings contained in the labeling approved, as well as the existence of a REMS, for setmelanotide by the FDA or the specific obligations imposed as a condition for marketing authorization imposed by other equivalent competent authorities in foreign jurisdictions, particularly by the European Commission;
- availability of alternative treatments, including a number of obesity therapies already approved or expected to be commercially launched in the near future;
- the size of the target patient population, and the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the ability of setmelanotide to treat the maximum range of pediatric patients, and any limitations on its indications for use, such as if the labeling limits the approved population to patients ages 12 and above;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning setmelanotide or competing products and treatments;
- pricing and cost effectiveness;
- the effectiveness of our sales and marketing strategies;
- our ability to increase awareness of setmelanotide through marketing efforts;
- our ability to obtain sufficient third-party coverage or reimbursement;
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage; and
- the likelihood that the FDA or other equivalent competent authorities in foreign jurisdictions may require development of a REMS as a condition of approval or post-approval, may not agree with our proposed REMS or may impose additional requirements that limit the promotion, advertising, distribution or sales of setmelanotide.

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

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

Currently, there are no approved or effective current treatments for regulating hunger and hyperphagia related behaviors of patients with POMC deficiency obesity, LepR deficiency obesity, Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, or POMC epigenetic disorders. Bariatric surgery is not a treatment option for these genetic disorders of obesity because the severe obesity and hyperphagia associated with these disorders are considered to be risk factors for bariatric surgery. While we are unaware of any competitive products in development

for the obesity and hyperphagia caused by MC4 pathway deficiencies specifically, new competitors may emerge which could limit our business opportunity in the future.

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

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

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

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

**Risks Related to Our Dependence on Third Parties**

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

We enter into agreements with third-party CROs to provide monitors for and to manage data for our ongoing clinical trials. We rely heavily on these parties for the execution of clinical trials for setmelanotide and control only certain aspects of their activities. As a result, we have less direct control over the conduct, timing and completion of these clinical

trials and the management of data developed through the clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. However, we remain responsible for the conduct of these trials and are subject to enforcement which may include civil and criminal liabilities for any violations of FDA rules and regulations and the comparable foreign regulatory provisions during the conduct of our clinical trials. Outside parties may:

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

These factors may materially adversely affect the willingness or ability of third parties to conduct our clinical trials and may subject us to unexpected cost increases that are beyond our control. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with current Good Clinical Practices, or cGCPs, which are guidelines enforced by the FDA, the Competent Authorities of the EU member states and equivalent competent authorities in foreign jurisdictions for any products in clinical development. The FDA enforces these regulations and cGCP guidelines through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we or our CROs fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or other equivalent competent authorities in foreign jurisdictions may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our clinical trials comply with cGCPs. In addition, our clinical trials must be conducted with products produced under current Good Manufacturing Practices, or cGMPs. Our failure or the failure of our CROs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action up to and including civil and criminal penalties.

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

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

We do not currently have, nor do we plan to acquire, the infrastructure or capability to internally manufacture our clinical drug supply of setmelanotide, or any future product candidates, for use in the conduct of our preclinical studies and clinical trials, and we lack the internal resources and the capability to manufacture any product candidate on a clinical or commercial scale. The facilities used by our contract manufacturing organizations, or CMOs, to manufacture the active pharmaceutical ingredient, or API, and final drug product must pass inspection by the FDA and other equivalent competent authorities in foreign jurisdictions pursuant to inspections that would be conducted after we submit our NDAs or relevant foreign regulatory submission to the other equivalent competent authorities in foreign jurisdictions. In addition, our clinical

trials must be conducted with products produced under cGMP regulations. Our failure or the failure of our CROs or CMOs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action, including civil and criminal penalties. If we import any drugs or drug substances, we would be subject to FDA and U.S. Bureau of Customs and Border Patrol, or CBP, import regulation requirements. Such enforcement for our failure or our CROs or CMOs' failure to comply with these regulations could result in import delays, detention of products, and, depending on criteria such as the history of violative activities, the FDA could place a foreign firm or certain drug substances or products on Import Alert and require that all such drug substances or products be subject to detention without physical examination, or DWPE, which could significantly impact the global supply chain for setmelanotide. FDARA provides that prescription drug products, with the exception of those on the FDA's drug shortage list or properly imported by individuals, may not be imported for commercial use if they were manufactured in a foreign country, unless they have been approved or are otherwise authorized to be marketed in the United States and are labeled accordingly.

We currently contract with a third party for the manufacture of setmelanotide and intend to continue to do so in the future. We have entered into a process development and manufacturing services agreement with Corden Pharma Brussels S.A, or Corden, formerly Peptisyntha SA prior to its acquisition by Corden, under which Corden will provide certain process development and manufacturing services in connection with the manufacture of setmelanotide. We have also entered into a process development and manufacturing services agreement with Recipharm Monts S.A.S, or Recipharm, under which Recipharm will provide certain process development and manufacturing services in connection with the manufacture of setmelanotide. Under our agreements, we pay both Corden and Recipharm for services in accordance with the terms of mutually agreed upon work orders, which we, Corden and Recipharm may enter into from time to time. The agreement with Corden also provides that, subject to certain conditions, for a period following each product launch date, we will source from Corden a portion of our requirements for that product being sourced from non-affiliate third parties. We may need to engage additional third-party suppliers to manufacture our clinical drug supplies. In the future, if we approach commercialization of setmelanotide or any future product candidate, we will need to engage other third parties to assist in, among other things, labeling, packaging, distribution, post-approval safety reporting, and pharmacovigilance activities. We cannot be certain that we can engage third-party suppliers on terms as favorable as those that are currently in place.

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

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

We do not have long-term supply agreements in place with our contractors, and each batch of setmelanotide is individually contracted under a quality and supply agreement. If we engage new contractors, such contractors must be approved by the FDA and other equivalent competent authorities in foreign jurisdictions. We will need to submit

information to the FDA and other equivalent competent authorities in foreign jurisdictions describing the manufacturing changes. If manufacturing changes occur post-approval, the FDA will have to approve these changes. We plan to continue to rely upon CMOs and, potentially, collaboration partners to manufacture commercial quantities of setmelanotide, if approved. Our current scale of manufacturing appears adequate to support all of our current needs for clinical trial supplies for setmelanotide. If setmelanotide is approved, we will need to identify CMOs or partners to produce setmelanotide on a larger scale.

**Risks Related to Our Intellectual Property Rights**

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

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

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. Although most of the patents and patent applications mentioned in the letter were abandoned or not in force at the time the letter was sent to us, and subsequent to our response, the third party has allowed three additional U.S. patents to lapse for non-payment of patent maintenance fees, we cannot assure you that the holder of these third-party patents will not attempt to assert these patents against us.

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

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

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

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

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

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

We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, such intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Our employees have been previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of the former employers of our employees. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. If we fail in defending such claims, in addition to paying money damages, we may lose valuable intellectual property rights or personnel. A loss of key personnel or their work product could hamper or prevent our ability to commercialize setmelanotide, which would materially adversely affect our commercial development efforts.

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

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

We currently have only one product candidate, setmelanotide, in clinical development, and our business depends entirely on its successful clinical development, regulatory approval and commercialization. We currently have no drug products for sale and may never be able to develop marketable drug products. Setmelanotide, which is currently in Phase 3 clinical development as a treatment for genetic deficiencies affecting the MC4 pathway, including POMC deficiency obesity and LepR deficiency obesity, will require substantial additional clinical development, testing and regulatory approval before we are permitted to commence commercialization. The clinical trials of setmelanotide are, and the manufacturing and marketing of setmelanotide will be, subject to extensive and rigorous review and regulation by numerous government authorities in the United States and in other countries where we intend to test and, if approved, market setmelanotide. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through non-clinical testing and clinical trials that the product candidate is safe and effective for use in each target indication. This process can take many years and approval, if any, may be conditional on post-marketing studies and surveillance, and will require the expenditure of substantial resources beyond the proceeds we raised from our IPO. 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 such countries. We have two Phase 3 clinical trials underway, one each for the treatment of POMC deficiency obesity and LepR deficiency obesity. Under our current development program, we plan to conduct a single Phase 3 clinical trial for POMC deficiency obesity. To date, in our ongoing discussions with the FDA, the agency has not asked for additional Phase 3 trials in POMC deficiency obesity, but the agency could still require us to conduct additional Phase 3 clinical trials for this indication. Moreover, for POMC deficiency obesity, the FDA could alter its previous advice on many aspects of the trial—the small size, the open label design, the amount of past medical history available on individual patients, the statistical analysis plan, the definition of clinically-relevant success for the protocol, entry of patients ages 12 or over—all of which may impact the timing and ability to obtain FDA approval. There are other aspects of the trial for which we have not received advice from the FDA, such as the number of U.S. versus non-U.S. patients and the number of patients with POMC gene defects versus the number of patients with PCSK1 defects, which could also impact the timing of and our ability to obtain FDA approval. We have not discussed the protocol for a Phase 3 program for LepR deficiency obesity with the FDA and thus we do not know if the FDA will provide advice on this trial that differs from the advice provided by the FDA for the trial in POMC deficiency obesity. Therefore, the timeline for enrollment, availability of data, and cost of conducting such trials are uncertain, and could be less favorable than those applicable to the POMC deficiency obesity program.

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

The FDA or other regulatory authorities and other equivalent competent authorities in foreign jurisdictions will also require that we conduct one or more pivotal trials for each other indication sought. In addition, we are not sure if one

or more Phase 3 trials would be required for approval in each other indication. The need and length of placebo-controlled data in these pivotal trials and the number of patients required for these approvals is also unclear. We expect to seek an indication for obesity caused by monogenic deficiencies affecting the MC4 pathway. We are currently conducting Phase 3 trials for treatment of setmelanotide in POMC deficiency obesity and LepR deficiency obesity and Phase 2 trials for treatment of Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders. If the clinical data meet key primary and secondary endpoints for safety and efficacy, our overall clinical program may be less time consuming and require fewer patients than might a program for a broader obesity indication.

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

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

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

Our plan is to expand our internal clinical development operations and capabilities so that we can continue to enroll and manage our Phase 2 clinical trials, and enroll and manage our Phase 3 clinical trials, such that, if the clinical trials are successful, we can file an NDA for POMC deficiency obesity in the United States by 2019. We believe we have finalized the design, timing and size of our Phase 3 trial for POMC deficiency obesity with the FDA but we cannot assure you that the trial will not be subject to further modification or that it will be completed on time. In addition, obtaining approval of an NDA and the approval of a marketing authorization application from the European Commission is a complex, lengthy, expensive and uncertain process, and the FDA, EMA or equivalent competent authorities in foreign jurisdictions may delay, limit or deny approval of setmelanotide for many reasons, including, among others:

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may disagree with our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials;

- we may not be able to demonstrate to the satisfaction of the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions that setmelanotide is safe and effective in treating obesity caused by certain genetic deficiencies affecting the MC4 pathway;

- the results of our clinical trials may not be interpretable or meet the level of statistical or clinical significance required by the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions for marketing approval. For example, the potential unblinding of setmelanotide studies due to easily identifiable adverse events may raise the concern that potential bias has affected the clinical trial results;

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may disagree with the number, size, conduct or implementation of our clinical trials;

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may require that we conduct additional clinical trials or pre-clinical studies;

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions or the applicable foreign regulatory agency may identify deficiencies in our chemistry, manufacturing or controls of setmelanotide;

- the CROs that we retain to conduct our clinical trials may take actions outside of our control that materially adversely impact our clinical trials;

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may find the data from preclinical studies and clinical trials insufficient to demonstrate that clinical and other benefits of setmelanotide outweigh its safety risks;

- the FDA, the EMA, or other equivalent competent authorities in foreign may disagree with our interpretation of data from our preclinical studies and clinical trials;

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may not approve the formulation, labeling or specifications of setmelanotide;

- the FDA, the EMA, or other equivalent competent authorities in foreign may not accept data generated at our clinical trial sites;

- if and when our NDA or our marketing authorization application is submitted and reviewed by an advisory committee, the FDA, the EMA, or the equivalent competent authorities in foreign jurisdictions may have difficulties scheduling an advisory committee meeting in a timely manner or the advisory committee may recommend against approval of our application or may recommend that the FDA, the EMA, or the equivalent competent authorities in foreign jurisdictions require, as a condition of approval, additional preclinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;

- the FDA may require development of a REMS as a condition of approval or post-approval, or may not agree with our proposed REMS or may impose additional requirements that limit the promotion, advertising, distribution, or sales of setmelanotide. In addition, the European Commission may grant only conditional approval marketing authorization or impose specific obligations as a condition for marketing authorization, or may require us to conduct post authorization safety studies as a condition of grant of marketing authorization;

- the FDA or other equivalent competent foreign regulatory agency may deem our manufacturing processes or our facilities or the facilities of our CMOs inadequate to preserve the identity, strength, quality, purity, or potency of our product; or

- the FDA, the European Commission, or the equivalent competent authorities in foreign jurisdictions may change its approval policies or adopt new regulations and guidance.

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

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

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

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

Even if we receive marketing approval for setmelanotide, regulatory authorities may impose significant restrictions on setmelanotide's indicated uses or marketing or impose ongoing requirements for potentially costly post approval studies. Setmelanotide will also be subject to ongoing requirements by the FDA, the EMA, and the competent authorities in the EU member states, governing labeling, packaging, storage advertising, promotion, marketing, distribution, importation, exportation, post-approval, manufacturing, recordkeeping, and submission of safety and other post market information. The FDA and the other competent foreign authorities haves 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, setmelanotide or the manufacturing facilities for setmelanotide fail to comply with applicable regulatory requirements, a regulatory agency may, among other things:

- issue warning letters or untitled letters;
- seek an injunction or impose civil or criminal penalties or monetary fines;

- suspend or withdraw marketing approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications submitted by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain setmelanotide, refuse to permit the import or export of setmelanotide, or request that we initiate a product recall.

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

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

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

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

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of setmelanotide, restrict or regulate post-approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any products for which we, or they, obtain marketing approval. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative

initiatives. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for any approved products.

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

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee does not apply to sales of certain products approved exclusively for orphan indications;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;

- expansion of manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;

- introduction of a price reporting requirement for drugs that are inhaled, instilled, implanted, injected, or infused and not generally dispensed through retail community pharmacies;

- addition of more entity types eligible for participation in the Public Health Service the 340B drug pricing program, or the 340B program;

- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;

- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;

- the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. However, the IPAB implementation has been not been clearly defined. ACA provided that under certain circumstances, IPAB recommendations or recommendations of the Secretary of Health and Human Services will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and

- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

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

approvals, may otherwise affect the prices we may obtain for setmelanotide or the frequency with which setmelanotide is prescribed or used if approved.

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

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

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

The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of setmelanotide to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.

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

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

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

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

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

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

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

For example, the FDA and other equivalent competent authorities in foreign jurisdictions strictly regulate the promotional claims that may be made about prescription products, such as setmelanotide, if approved. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in

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

In the European Union, the advertising and promotion of our products are subject to EU laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual EU member states may apply to the advertising and promotion of medicinal products. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities. The SmPC is the document that provides information to physicians concerning the safe and effective use of the medicinal product. It forms an intrinsic and integral part of the marketing authorization granted for the medicinal product. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion. The off-label promotion of medicinal products is prohibited in the European Union. The applicable laws at European Union level and in the individual EU member states also prohibit the direct-to-consumer advertising of prescription-only medicinal products. Violations of the rules governing the promotion of medicinal products in the European Union could be penalized by administrative measures, fines and imprisonment. These laws may further limit or restrict the advertising and promotion of our products to the general public and may also impose limitations on our promotional activities with health care professionals.

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

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

- The United States federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, or receiving remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease order or arranging for or recommending of the purchase, lease or order of any good or service for which payment may be made, in whole or in part, by federal healthcare programs such as Medicare and Medicaid. This statute has been interpreted to apply to arrangements between pharmaceutical companies on one hand and prescribers, purchasers and formulary managers on the other. Liability under the Anti-Kickback Statute may be established without proving actual knowledge of the statute or specific intent to violate it. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. Although there are a number of statutory exemptions and regulatory safe harbors to the federal Anti-Kickback Statute protecting certain common business arrangements and activities from prosecution or regulatory sanctions, the exemptions and safe harbors are drawn narrowly. Practices that involve remuneration to those who prescribe, purchase, or recommend pharmaceutical and biological products, including certain discounts, or engaging such individuals as consultants, advisors, or speakers, may be subject to scrutiny if they do not fit squarely within an exemption or safe harbor. Our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability. Moreover, there are

no safe harbors for many common practices, such as educational and research grants, charitable donations, product support and patient assistance programs.

- The federal civil False Claims Act prohibits individuals or entities from, among other things, knowingly presenting, or causing to be presented a false or fraudulent claim for payment of government funds, or knowingly making, using or causing to made or used a false record or statement material to an obligation to pay money to the government or knowingly concealing or knowingly and improperly avoiding, decreasing or concealing an obligation to pay money to the federal government. Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Many pharmaceutical manufacturers have been investigated and have reached substantial financial settlements with the federal government under the civil False Claims Act for a variety of alleged improper activities including causing false claims to be submitted as a result of the marketing of their products for unapproved and thus non-reimbursable uses, inflating prices reported to private price publication services which are used to set drug payment rates under government healthcare programs, and other interactions with prescribers and other customers including those that may have affected their billing or coding practices and submission to the federal government. The government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. Pharmaceutical and other healthcare companies also are subject to other federal false claims laws, including, among others, federal criminal healthcare fraud and false statement statutes that extend to non-government health benefit programs.

- The federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.

- HIPAA and the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statement or entry in connection with the delivery of or payment for healthcare benefits, items or services.

- Numerous federal and state laws and regulations that address privacy and data security, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the FTC Act), govern the collection, use, disclosure and protection of health-related and other personal information.

- The federal transparency requirement known as the federal Physician Payments Sunshine Act, being implemented as the Open Payments Program, requires certain manufacturers of drugs, devices, biologics and medical supplies to report payments and other transfers of value to physicians and teaching hospitals, as well as ownership and investments interests held by physicians and their immediate family members. Pharmaceutical and biological manufacturers with products for which payment is available under Medicare, Medicaid or the State Children’s Health Insurance Program are required to submit a report to the Centers for Medicare and Medicaid Services within the U.S. Department of Health and Human Services on or before the 90th day of each calendar year disclosing reportable payments made in the previous calendar year.

- Analogous state laws and regulations, such as state anti-kickback and false claims laws, which may apply to items or services reimbursed under Medicaid and other state programs or, in several states, regardless of the payer. Some state laws also require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products and to report gifts and payments to certain health care providers in those states. Some of these states also prohibit certain marketing-related activities including the provision of gifts, meals, or other items to certain health care providers. In addition, California, Connecticut, Nevada, and Massachusetts require pharmaceutical companies to implement compliance programs or marketing codes of conduct.

Ensuring that our business arrangements and interactions with healthcare professionals, third-party payors, patients and others comply with applicable healthcare laws and regulations will require substantial resources. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including anticipated activities to be conducted by our sales and marketing team, were found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines and exclusion from government funded healthcare programs, such as Medicare and Medicaid, the curtailment or restructuring of our operation, any of which could substantially disrupt our operations. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws or regulations, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing or selling certain product candidates and products outside of the United States, which could limit our growth potential and increase our development costs.

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

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

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

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

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

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

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

The Trump administration has taken several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. On January 30, 2017, President Trump issued an executive order, applicable to all executive agencies, including the FDA, that requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This executive order includes a budget neutrality

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

**Risks Related to Employee Matters and Managing Growth**

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

We are highly dependent on Keith M. Gottesdiener, M.D., our Chief Executive Officer and President, Hunter Smith, our Chief Financial Officer and Treasurer, Nithya Desikan, our Chief Commercial Officer, Lex H.T. Van der Ploeg, Ph.D., our Chief Scientific Officer, and Fred T. Fiedorek, M.D., our Chief Medical Officer. We have employment agreements with these individuals that became effective upon consummation of our IPO, 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.***

As a public company, we expect to increase our number of employees and the scope of our operations. In particular, we will need to transition from a research and development company to a commercial company. To manage our anticipated development and expansion, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Also, our management may need to divert a disproportionate amount of its attention away from their day-to-day activities and devote a substantial amount of time to managing these development activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, and give rise to operational mistakes, loss of business and commercial opportunities, loss of employees and reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of setmelanotide. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize setmelanotide, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our company.

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

As a newly public company, we 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 control over matters subject to stockholder approval.***

Based on the number of shares outstanding as of September 30, 2017, after the closing our IPO in October 2017, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately 64.1% of our voting stock. These stockholders will have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control 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.***

Prior to our IPO, there had been no public market for shares of our common stock. Our stock only recently began trading on The NASDAQ Global Market, but 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 does not develop or 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.

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

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us, our business, our market or our competitors. We do not control these analysts. We currently have very limited research coverage by securities and industry analysts. If no additional securities or industry analysts commence 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.

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

The market price for our common stock is likely to be volatile and may fluctuate significantly in response to a number of factors, most of which we cannot control, including, among others:

- plans for, progress of, or results from preclinical studies and clinical trials of setmelanotide;
- the failure of the FDA to approve setmelanotide;
- announcements of new products, technologies, commercial relationships, acquisitions or other events by us or our competitors;
- the success or failure of other weight loss therapies and companies targeting rare diseases and orphan drug treatment;
- regulatory or legal developments in the United States and other countries;

- failure of setmelanotide, if approved, to achieve commercial success;
- fluctuations in stock market prices and trading volumes of similar companies;
- general market conditions and overall fluctuations in U.S. equity markets;
- variations in our quarterly operating results;
- changes in our financial guidance or securities analysts' estimates of our financial performance;
- changes in accounting principles;
- our ability to raise additional capital and the terms on which we can raise it;
- sales of large blocks of our common stock, including sales by our executive officers, directors and significant stockholders;
- additions or departures of key personnel;
- discussion of us or our stock price by the press and by online investor communities; and
- other risks and uncertainties described in these risk factors.

***Our quarterly operating results may fluctuate significantly.***

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

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

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

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

We will have considerable discretion in the application of the net proceeds from our IPO. We intend 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, the preparation for commercialization of setmelanotide, initiatives to expand the diagnosis of genetic obesity, including research and scientific exchange related to our ongoing genotyping and genetic epidemiology studies and for working capital and general administrative expenses, additional research and development expenses, and other general corporate purposes. As a result, investors will be relying upon management's judgment with only limited information about our specific intentions for the use of the net proceeds. 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 that provision, we can carry forward certain taxable losses of our subsidiaries to offset future taxable income, if any, until such losses are used or expire. The same is true of other unused tax attributes, such as research tax credits. As of December 31, 2016, we had approximately $46.9 and $24.4 million of unused federal and state carryforwards of NOLs, respectively, and approximately $1.0 and $0.4 million of unused federal and state carryforwards of tax credits, respectively.

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

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

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

We may seek additional capital through a combination of private and public equity offerings, debt financings, collaborations and strategic and licensing arrangements. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, a stockholder's ownership interest in our company will be diluted. In addition, the terms of any such securities may include liquidation or other preferences that materially adversely affect the rights of our stockholders. Debt financing, if available, would increase our fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaboration, strategic partnerships and licensing arrangements with third parties, we may have to relinquish valuable

rights to setmelanotide, our intellectual property or future revenue streams, or grant licenses on terms that are not favorable to us.

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

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market after the lock-up and other legal restrictions on resale lapse, the trading price of our common stock could decline. Based upon the number of shares outstanding as of September 30, 2017, and after giving effect to the closing of our IPO in October 2017, we had outstanding a total of approximately 27.3 million shares of common stock. Of these shares, approximately 7.2 million of the shares of our common stock sold in the IPO are freely tradable, without restriction, in the public market.

The lock-up agreements pertaining to our IPO will expire on April 2, 2018, following which up to an additional 19.2 million shares of common stock will be eligible for sale in the public market, of which approximately 13.0 million shares are held by current directors, executive officers and their respective affiliates and may be subject to Rule 144 under the Securities Act. The underwriters from our IPO may, however, in their sole discretion, permit our officers, directors and other stockholders who are subject to these lock-up agreements to sell or transfer shares prior to the expiration of the lock-up agreements.

In addition, approximately 4.0 million shares of our common stock that are either subject to outstanding stock awards or reserved for future issuance under our 2017 Plan are eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

The holders of approximately 18.9 million shares of our common stock, or approximately 69.1% of our total outstanding common stock as of September 30, 2017 and after giving effect to the issuance of shares in our IPO, will be entitled to rights with respect to the registration of their shares under the Securities Act, subject to vesting schedules and to the lock-up agreements described above. 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) the last day of the fiscal year (a) following the fifth anniversary of the completion of our IPO, (b) in which we have total annual gross revenue of at least $1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior

June 30th, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

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

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

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

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.

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

*Unregistered Sales of Equity Securities*

During the quarter ended September 30, 2017, we issued and sold the following unregistered securities:

On August 18, 2017 we issued 20,474,998 shares of series A preferred stock, $0.001 par value per share, to a number of accredited investors for $1.00 per share. These shares were issued in reliance on Regulation D, Rule 506 and/or Rule 4(2) under the Securities Act.

We granted options under the 2015 Plan to purchase an aggregate of 540,996 shares of our common stock to employees, consultants and directors, having exercise prices ranging from $6.88 to $8.44 per share which issuances were exempt from registration under Rule 701 under the Securities Act. During this period, 152,671 stock options were exercised.

***Use of Proceeds***

On September 25, 2017, the SEC declared effective our registration statement on Form S-1 (File No. 333-220327), as amended, filed in connection with our IPO. The IPO closed on October 10, 2017 and we issued and sold 8,107,500 shares of our common stock at a price to the public of $17.00 per share, which included the exercise in full of the underwriters' option to purchase 1,057,500 additional shares. We received gross proceeds from the IPO of approximately $137.8 million, before deducting underwriting discounts and commissions of approximately $9.6 million, and estimated offering expenses of approximately $2.4 million. Morgan Stanley, Bank of America Merrill Lynch, Cowen Inc. and Needham & Company acted as book-running managers for the offering. No offering expenses were paid or are payable, directly or indirectly, to our directors or officers, to persons owning 10% or more of any class of our equity securities or to any of our affiliates.

The net proceeds from the IPO have been invested in United States treasury money market funds. There has been no material change in the expected use of the net proceeds from our IPO as described in our registration statement on Form S-1.

***Issuer Purchases of Equity Securities***

We did not repurchase any of our equity securities during the three months ended September 30, 2017.

**Item 3. Defaults Upon Senior Securities**

Not applicable.

**Item 4. Mine Safety Disclosure**

Not applicable.

**Item 5. Other Information**

None

**Item 6. Exhibits**

| Exhibit Number | Exhibit Description | Incorporated by Reference | | |
|---|---|---|---|---|
| | | Form | Date | Number |
| 3.1 | Amended and Restated Certificate of Incorporation. | S-1/A | 9-25-2017 | 3.3 |
| 3.2 | Amended and Restated Bylaws. | S-1/A | 9-25-2017 | 3.5 |
| 4.1 | Form of Common Stock Certificate. | S-1/A | 9-25-2017 | 4.1 |
| 4.2 | Amended and Restated Investors' Rights Agreement, dated August 21, 2017. | S-1 | 9-5-2017 | 4.2 |
| 10.1 | Form of Indemnification Agreement. | S-1/A | 9-25-2017 | 10.1 |
| 10.2*† | 2017 Equity Incentive Plan and Form of Option Agreement and Notice of Exercise. | | | |
| 10.3† | Offer Letter, dated November 16, 2016, by and between the Registrant and Bart Henderson. | S-1 | 9-5-2017 | 10.3 |
| 10.4† | Offer Letter, dated November 16, 2016, by and between the Registrant and Keith M. Gottesdiener. | S-1 | 9-5-2017 | 10.4 |
| 10.5† | Offer Letter, dated November 16, 2016, by and between the Registrant and Fred T. Fiedorek. | S-1 | 9-5-2017 | 10.5 |
| 10.6 | License Agreement, dated March 21, 2013, by and between the Registrant (f/k/a Rhythm Metabolic, Inc.) and Ipsen Pharma S.A.S. | S-1 | 9-5-2017 | 10.6 |
| 10.7 | Development and Manufacturing Services Agreement, dated July 17, 2013, by and between the Registrant (f/k/a Rhythm Metabolic, Inc.) and Peptisyntha Inc. (n/k/a Corden Pharma International). | S-1 | 9-5-2017 | 10.7 |
| 10.8 | License Agreement dated January 4, 2016, by and between the Registrant and Camurus AB | S-1 | 9-5-2017 | 10.8 |
| 10.9 | Amended and Restated Payroll Services Agreement, dated March 21, 2013, by and between the Registrant (f/k/a Rhythm Metabolic, Inc.) and Rhythm Pharmaceuticals, Inc. | S-1 | 9-5-2017 | 10.9 |
| 10.10*† | Rhythm Pharmaceuticals, Inc. 2017 Employee Stock Purchase Plan. | | | |
| 10.11 | Lease, dated November 25, 2015, by and between 500 Boylston & 222 Berkeley Owner (DE) LLC and the Registrant. | S-1 | 9-5-2017 | 10.11 |
| 10.12 | Consulting Agreement, dated June 12, 2017, by and between the Registrant and Bart Henderson. | S-1 | 9-5-2017 | 10.12 |
| 10.13† | Offer Letter, dated September 13, 2017, by and between the Registrant and Keith M. Gottesdiener. | S-1/A | 9-25-2017 | 10.13 |
| 10.14† | Offer Letter, dated September 13, 2017, by and between the Registrant and Fred T. Fiedorek. | S-1/A | 9-25-2017 | 10.14 |

| | | | | |
|---|---|---|---|---|
| 10.15 | Development and Manufacturing Services Agreement, dated as of December 21, 2016, by and between Registrant and Recipharm Monts S.A.S. | S-1 | 9-5-2017 | 10.15 |
| 10.16† | Offer Letter, dated September 13, 2017, by and between the Registrant and Hunter Smith. | S-1/A | 9-25-2017 | 10.18 |
| 10.17† | Offer Letter, dated September 13, 2017, by and between the Registrant and Nithya Desikan. | S-1/A | 9-25-2017 | 10.19 |
| 10.18† | Summary of Non-Employee Director Compensation Policy. | S-1 | 9-5-2017 | 10.20 |
| 10.19† | 2015 Equity Incentive Plan and Form of Option Agreement and Notice of Exercise. | S-1/A | 9-25-2017 | 10.21 |
| 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 herewith

† Indicates management contract or compensatory plan

**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 14, 2017

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

Dated: November 14, 2017

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

**Exhibit 10.10**

# RHYTHM PHARMACEUTICALS, INC.

# 2017 EMPLOYEE STOCK PURCHASE PLAN

**RHYTHM PHARMACEUTICALS, INC.**

**2017 Employee Stock Purchase Plan**

## 1. Purpose and History

The purpose of this Plan is to give Employees wishing to do so a convenient means of purchasing Common Stock of the Company through payroll deductions. The Company believes that ownership of Common Stock by Employees will foster greater Employee interest in the Company's growth and development.

This Plan was adopted by the Board on September 29, 2017. It is the Company's intention that the Plan qualify as an "employee stock purchase plan" under Section 423 of the Code. The provisions of the Plan shall, accordingly, be construed in a manner consistent with the requirements of that Code section.

## 2. Definitions

As used in this Plan, the following terms shall have the following meanings:

2.1. Board means the Company's Board of Directors.

2.2. Business Day means a day on which the NASDAQ Stock Market (or any other national securities exchange on which the Common Stock is then listed) is open for trading. Every date under this Plan that falls on a weekend, a holiday or any other day that is not a Business Day (and any event that occurs after 5 p.m. eastern time on any date) shall be deemed automatically to fall on the next Business Day.

2.3. Code means the Internal Revenue Code of 1986, as amended from time to time, or any successor statute thereto, and any regulations issued from time to time thereunder.

2.4. Commission means the U.S. Securities and Exchange Commission.

2.5. Committee means the Compensation Committee of the Board or such other committee delegated responsibility by the Board for the administration of the Plan, as provided in Section 4 of the Plan. For any period during which no such committee is in existence "Committee" shall mean the Board and all authority and responsibility assigned to the Committee under the Plan shall be exercised, if at all, by the Board.

2.6. Common Stock or Stock means the common stock, par value $0.001 per share, of the Company.

2.7. Company means Rhythm Pharmaceuticals, Inc., a corporation organized under the laws of the State of Delaware.

2.8. Compensation means an Employee's total compensation, including base pay or regular earnings plus commissions, bonuses, and overtime.

2.9. Continuous Status as an Employee means the absence of any interruption or termination of service as an Employee. Continuous Status as an Employee shall not be considered interrupted in the case of (i) sick leave; (ii) military leave; (iii) any other leave of absence approved

by the Plan administrator, provided that such leave is for a period of not more than three months, unless reemployment upon the expiration of such leave is guaranteed by contract or statute, or unless provided otherwise pursuant to Company policy adopted from time to time; or (iv) transfers between locations of the Company or between the Company and a Covered Entity.

2.10. Contributions means all amounts credited to the account of a Participating Employee pursuant to the Plan.

2.11. Corporate Transaction means any (1) merger or consolidation of the Company with or into another entity as a result of which the Stock of the Company is converted into or exchanged for the right to receive cash, securities or other property or is cancelled, (2) sale or exchange of Stock of the Company possessing more than fifty percent (50%) of the total combined voting power of the Company's outstanding securities for cash, securities or other property, (3) sale, transfer, or other disposition of all or substantially all of the Company's assets to one or more other persons in a single transaction or series of related transactions or (4) liquidation or dissolution of the Company; except, in the case of clauses (1) and (2), for a transaction the principal purpose of which is to change the state in which the Company is incorporated.

2.12. Covered Entity means any Subsidiary (whether now existing or subsequently established or acquired) that may adopt the Plan from time to time in accordance with the procedures set forth in Section 14 hereof with the Company's consent.

2.13. Effective Date means the IPO Date.

2.14. Employee means an employee of the Company or a Covered Entity who is customarily employed for at least 20 hours per week and more than five months in a calendar year. The Committee may, prior to the start of the applicable Plan Period, waive one or both of the twenty (20) hour and five (5) month service requirements and/or establish such other eligibility requirements as it deems appropriate.

2.15. Exchange Act means the Securities Exchange Act of 1934, as amended.

2.16. Fair Market Value has the meaning set forth in Section 6.4(c).

2.17. Initial Plan Period means the first Plan Period of the Plan.

2.18. IPO Date means the date of the closing of the initial public offering of shares of Common Stock.

2.19. New Plan Period Termination Date has the meaning set forth in Section 12.4.

2.20. Participating Employee means an Employee who elects to participate in the Plan pursuant to Section 6.2(b).

2.21. Plan means this Rhythm Pharmaceuticals, Inc. 2017 Employee Stock Purchase Plan.

2.22. Plan Period Commencement Date means the first business day of each Plan Period.

2.23. Plan Period Termination Date means the last business day of each Plan Period.

2.24. Plan Period means each successive period described in Section 6.1, at the end of which each Participating Employee (whose participation has not terminated pursuant to Section 6.7) shall purchase Shares.

2.25. Securities Act means the Securities Act of 1933, as amended.

2.26. Purchase Price means with respect to a Plan Period an amount equal to or greater than eighty five percent (85%) of the Fair Market Value of a Share on the Plan Period Commencement Date or on the Plan Period Termination Date, whichever is lower.

2.27. Share means a share of Common Stock, as adjusted in accordance with Section 12 of the Plan.

2.28. Subsidiary means a corporation, in an unbroken chain of corporations beginning with the Company if, at the time of the granting of the option, each of the corporations other than the last corporation in the unbroken chain owns stock possessing fifty percent (50%) or more of the total combined voting power of all classes of stock in one of the other corporations in such chain.

**3. Shares Reserved For The Plan**

Subject to adjustment as provided in Section 12 hereof, the number of Shares reserved for issuance hereunder shall be two hundred seventy-two thousand, eight hundred forty-one (272,841), provided, however, that the number of Shares authorized under this Section 3 of the Plan will be increased each January 1, commencing on January 1 of the year following the year in which the IPO Date occurs and ending on (and including) January 1, 2027, by an amount equal to the lesser of (i) one percent (1.0%) of outstanding Shares as of the end of the immediately preceding fiscal year and (ii) six hundred eighty-two thousand, one hundred two (682,102). Notwithstanding the foregoing, the Board may act prior to January 1 of a given year to provide that there will be no such January 1 increase in the number of Shares authorized under this Section 3 of the Plan for such year or that the increase in the number of Shares authorized under this Section 3 of the Plan for such year will be a lesser number than would otherwise occur pursuant to the preceding sentence. For purposes of applying the foregoing limitation, if any option expires, terminates or is cancelled for any reason without having been exercised in full, the Shares not purchased or received by the Employee shall again be available for options to be granted under the Plan. Shares issued pursuant to the Plan may be either authorized but unissued shares or shares held by the Company in its treasury.

**4. Administration**

The Plan shall be administered by the Committee, *provided, however*, that at any time and on any one or more occasions the Board may itself exercise any of the powers and responsibilities assigned to the Committee under the Plan and when so acting shall have the benefit of all of the provisions of the Plan pertaining to the Committee's exercise of its authority hereunder; and *provided, further*, that the Committee may delegate its duties in order to facilitate the purchase and transfer of Shares and to provide for the day-to-day administration of the Plan with all powers necessary to enable the delegate to carry out its duties in that respect. Subject to the provisions of the Plan, the Committee shall have complete authority, in its discretion, to make or to select the manner of making all determinations with respect to each option to be granted by the Company under the Plan. In making such determinations, the Committee may take into account such factors

as the Committee in its discretion shall deem relevant. Subject to the provisions of the Plan, the Committee shall also have complete authority to interpret the Plan, to prescribe, amend and rescind rules and regulations relating to it and to make all other determinations necessary or advisable for the administration of the Plan. The Committee's determinations made in good faith on matters referred to in the Plan shall be final, binding and conclusive on all persons having or claiming any interest under the Plan or an option granted pursuant hereto.

**5. Eligibility for Awards**

Subject to the requirements of Section 6.2 and the limitations imposed by Section 423(b) of the Code, any Employee shall be eligible to participate in a Plan Period under the Plan as of the applicable Plan Period Commencement Date. Notwithstanding any provision of the Plan to the contrary, no Employee shall be granted an option under the Plan (i) if, immediately after the grant, such Employee (taking into account stock which would be attributed to such Employee pursuant to Section 424(d) of the Code) would own capital stock of the Company and/or hold outstanding options to purchase stock possessing five percent (5%) or more of the total combined voting power or value of all classes of stock of the Company or of any Subsidiary of the Company, or (ii) if such option would permit his or her rights to purchase stock under all employee stock purchase plans (described in Section 423 of the Code) of the Company and its Subsidiaries to accrue at a rate which exceeds twenty-five thousand dollars ($25,000) of such stock (determined on the basis of the Fair Market Value of such stock on the date or dates such option was granted) for each calendar year in which such option is outstanding at any time.

**6. Terms of Participation**

6.1. Plan Periods. The Initial Plan Period shall commence on May 1 or November 1 of such calendar year as the Committee may determine in its sole discretion and continue for six months. After the Initial Plan Period, there will be two consecutive six-month Plan Periods during each twelve month period thereafter, with the first six-month Plan Period beginning on May 1 and ending on the immediately following October 31, and the second six-month Plan Period beginning on November 1 and ending on the immediately following April 30 unless otherwise determined by the Committee.

6.2. Election to Participate and Plan Deductions.

(a) Shares shall be offered for purchase under the Plan through a series of successive, non-overlapping Plan Periods until such time as (i) the maximum number of Shares available for issuance under the Plan shall have been purchased or (ii) the Plan shall have been sooner terminated. At any time and from time to time, the Committee may change the duration and/or the frequency of Plan Periods or suspend operation of the Plan with respect to Plan Periods not yet commenced.

(b) An eligible Employee may become a Participating Employee in the Plan by completing an enrollment agreement provided by the Company and filing it with the Company at least three business days prior to the Plan Period Commencement Date for the Plan Period in which such Employee desires to participate, unless either an earlier or later time for filing the enrollment agreement is set by the Committee for all eligible Employees with respect to a given Plan Period. The enrollment agreement shall set forth the percentage of the Employee's Compensation (subject to Section 6.2(c) below) to be paid as Contributions pursuant to the Plan. Payroll deductions shall commence on the first payroll following the Plan Period Commencement

Date and shall end on the last payroll paid on or prior to the Plan Period Termination Date, unless sooner terminated by the Participating Employee as provided in Section 6.7.

(c) A Participating Employee may elect to have payroll deductions taken from each payroll during any Plan Period in an amount, in whole percentages, not less than one percent (1%) and not more than fifteen percent (15%) (or such other percentage as the Committee may establish from time to time before any Plan Period Commencement Date) of such Participating Employee's Compensation on each payroll date during the Plan Period. All payroll deductions made by a Participating Employee shall be credited to his or her account under the Plan. No interest shall accrue on Contributions to the Plan. A Participating Employee may not make any additional payments into such account.

(d) Unless the Committee announces otherwise before the start of a particular Plan Period, an eligible Employee's enrollment agreement in effect at the end of one Plan Period will remain in effect for each subsequent Plan Period.

(e) A Participating Employee may discontinue his or her participation in the Plan as provided in Section 6.7. A Participating Employee may, at any time during the Plan Period, reduce the rate of his or her payroll deduction to become effective as soon as administratively possible after filing the appropriate form with the Committee. The Participating Employee may not, however, effect more than one (1) such reduction per Plan Period. A Participating Employee may choose to increase his or her payroll deductions at any time during the specified enrollment period communicated to employees prior to the start of a Plan Period to be effective with that Plan Period.

(f) Notwithstanding the foregoing, to the extent necessary to comply with Section 423(b)(8) of the Code and Section 5 hereof, a Participating Employee's payroll deductions may be decreased during any Plan Period to zero percent (0%). Payroll deductions reduced to zero percent (0%) in compliance with this Section 6.2(f) shall re-commence automatically at the rate provided in such Participating Employee's enrollment agreement at the beginning of the next Plan Period, unless terminated by the Participating Employee as provided in Section 6.7.

(g) Any amounts left over in a Participating Employee's account upon expiration or termination of the Plan (or upon a withdrawal by a Participating Employee or upon a Participating Employee purchasing the maximum dollar amount or number of shares hereunder) shall be returned to the Participating Employee.

6.3. Shares.

(a) If the Committee determines that, on a given Plan Period Termination Date, the number of shares with respect to which options are to be exercised may exceed (i) the number of Shares that were available for sale under the Plan on the Plan Period Commencement Date, or (ii) the number of shares available for sale under the Plan on such Plan Period Termination Date, then the Company shall make a pro rata allocation of the Shares available for purchase on such Plan Period Termination Date in as uniform a manner as shall be practicable and as it shall determine in its sole discretion to be equitable among all Participating Employees exercising options to purchase Common Stock on such Plan Period Termination Date. The Company shall make a pro rata allocation of the Shares available on the Plan Period Commencement Date pursuant to the preceding sentence, notwithstanding any authorization of additional Shares for issuance under the Plan by the Company's stockholders subsequent to such Plan Period Commencement

Date.

(b) The Participating Employee shall have no interest or voting right in Shares covered by his or her option until such option has been exercised.

(c) Shares to be delivered to a Participating Employee under the Plan will be registered in the name of the Participating Employee.

6.4. Grant of Options.

(a) A Participating Employee shall be granted a separate option for each Plan Period in which he or she participates. The option shall be granted on the Plan Period Commencement Date for the Plan Period and shall provide the Participating Employee with the right to purchase Shares upon the terms set forth below.

(b) The number of Shares purchasable by a Participating Employee on each Plan Period Termination Date during the Plan Period, pursuant to Section 6.5 below, shall be determined by dividing such Employee's Contributions accumulated during such Plan Period up to such Plan Period Termination Date and credited to the Participating Employee's account as of the Plan Period Termination Date by the applicable Purchase Price. However, the maximum number of Shares a Participating Employee may purchase during each Plan Period shall not exceed 3,000 Shares, or such other number as may be determined by the Committee and announced to Employees at least five days prior to the scheduled beginning of the next Plan Period to be affected by the Committee's determination, provided that such purchase shall be subject to the limitations set forth in Section 6.2(c).

(c) The fair market value of the Shares on a given date (the "Fair Market Value") means the value of a share of Common Stock on a particular date determined by such methods or procedures as may be established by the Committee. Unless otherwise determined by the Committee, the Fair Market Value of the Common Stock as of any date, is (a) the closing price for the Common Stock as reported by the NASDAQ Stock Market (or on any other national securities exchange on which the Common Stock is then listed) for that date or, if no closing price is reported for that date, the closing price on the next preceding date for which a closing price was reported or (b) if the Common Stock is not traded on a national securities exchange but is traded over-the-counter, the closing or last price of the Common Stock on the composite tape or other comparable reporting system on that date or, if such date is not a trading day, the last market trading day prior to such date.

6.5. Exercise. Unless a Participating Employee withdraws from the Plan as provided in Section 6.7, each option shall be exercised automatically on each Plan Period Termination Date, and Shares shall accordingly be purchased on behalf of each Participating Employee on each such Plan Period Termination Date. The purchase shall be effected by applying the Participating Employee's payroll deductions for the Plan Period ending on such Plan Period Termination Date to the purchase of Shares (subject to the limitation on the maximum number of Shares purchasable per Participating Employee on any one Plan Period Termination Date) at the Purchase Price in effect for the Participating Employee for that Plan Period Termination Date. The Shares purchased upon exercise of an option hereunder shall be deemed to be transferred to the Participating Employee on the Plan Period Termination Date. During his or her lifetime, a Participating Employee's option to purchase Shares hereunder is exercisable only by him or her.

6.6. Delivery. As promptly as practicable after each Plan Period Termination Date, the Company shall arrange for the delivery to each Participating Employee of a certificate or certificates or book-entry authorization and instruction to the Company's transfer agent and registrar for the number of Shares purchased upon exercise of his or her option.

6.7. Voluntary Withdrawal; Termination of Employment.

(a) A Participating Employee may withdraw all but not less than all of the Contributions credited to his or her account under the Plan up to two weeks prior to the Plan Period Termination Date by giving written notice to the Company in accordance with the Company's policy regarding withdrawal from the Plan. All of the Participating Employee's Contributions credited to his or her account will be paid to him or her promptly after receipt of his or her notice of withdrawal and his or her option for the current Plan Period will be automatically terminated, and no further Contributions for the purchase of Shares will be made (or will be permitted to be made) during the Plan Period.

(b) Upon termination of the Participating Employee's Continuous Status as an Employee prior to a Plan Period Termination Date for any reason, including retirement or death, the Contributions credited to his or her account will be returned to him or her or, in the case of his or her death, to the person or persons entitled thereto under Section 8, and his or her option will be automatically terminated.

(c) In the event a Participating Employee fails to remain an eligible Employee during the Plan Period in which he or she is a Participating Employee, he or she will be deemed to have elected to withdraw from the Plan and the Contributions credited to his or her account and remaining there will be returned to him or her and his or her option terminated.

(d) A Participating Employee's withdrawal during a Plan Period will not have any effect upon his or her eligibility to participate in a succeeding Plan Period or in any similar plan which may hereafter be adopted by the Company.

**7. No Special Service Rights**

Nothing contained in this Plan shall confer upon any Employee any right with respect to the continuation of his or her employment with the Company or any Covered Entity or any other entity, corporation, partnership, limited liability company or business trust controlling, controlled by or under common control with the Company, or interfere in any way with the right of any such entity, subject to the terms of any separate employment agreement or provision of law or the Company's charter or by-laws to the contrary, at any time to terminate such employment relationship or to increase or decrease, or otherwise adjust, the other terms and conditions of the Employee's employment.

**8. Designation of Beneficiary**

8.1. A Participating Employee may file a written designation of a beneficiary who is to receive any Shares and cash, if any, from the Participating Employee's account under the Plan in the event of such Participating Employee's death subsequent to the end of a Plan Period but prior to delivery to him or her of such Shares and cash. Any such beneficiary shall also be entitled to receive any cash from the Participating Employee's account under the Plan in the event of such Participating Employee's death during a Plan Period.

8.2. Such designation of beneficiary may be changed by the Participating Employee at any time by written notice. In the event of the death of a Participating Employee and in the absence of a beneficiary validly designated under the Plan who is living at the time of such Participating Employee's death, the Company shall deliver such Shares and/or cash to the executor or administrator of the estate of the Participating Employee, or if no such executor or administrator has been appointed (to the knowledge of the Company), the Company, in its discretion, may deliver such Shares and/or cash to the spouse or to any one or more dependents or relatives of the Participating Employee, or if no spouse, dependent or relative is known to the Company, then to such other person as the Company may designate.

**9. Transferability of Options and Shares**

Neither Contributions credited to a Participating Employee's account nor any rights with regard to the exercise of an option or to receive Shares under the Plan may be assigned, transferred, pledged or otherwise disposed of in any way (other than by will, the laws of descent and distribution, or as provided in Section 8) by the Participating Employee. Any such attempt at assignment, transfer, pledge or other disposition shall be without effect, except that the Company may treat such act as an election to withdraw funds in accordance with Section 6.7. In addition, if the Committee has so announced to Participating Employees at least five days prior to the scheduled beginning of the next Plan Period, any Shares acquired on the Plan Period Termination Date of such Plan Period may be subject to restrictions specified by the Committee on the transfer of such Shares. Any Participating Employee selling or transferring any or all of his or her Shares purchased pursuant to the Plan must provide written notice of such sale or transfer to the Company within five business days after the date of sale or transfer. Such notice to the Company shall include the gross sales price, if any, the Plan Period during which the Shares being sold were purchased by the Participating Employee, the number of Shares being sold or transferred and the date of sale or transfer. The Committee may also require that Shares acquired under the Plan be deposited directly into an account established in the name of the Participating Employee with a Company-designated broker and be retained with such designated broker for a specified period of time.

**10. Use of Funds**

All Contributions received or held by the Company under the Plan may be used by the Company for any corporate purpose, and the Company shall not be obligated to segregate such Contributions from its other assets.

**11. Reports**

Individual accounts will be maintained for each Participating Employee in the Plan. Statements of account will be given to Participating Employees at least annually, which statements will set forth, with respect to the immediately prior calendar year, the amounts of Contributions, the per Share Purchase Price, the number of Shares purchased and the remaining cash balance, if any.

**12. Adjustments Upon Changes in Capitalization; Corporate Transactions**

12.1. Adjustment in General. All of the share numbers set forth in the Plan reflect the capital structure of the Company as of the Effective Date. If subsequent to that date the outstanding Shares (or any other securities covered by the Plan by reason of the prior application of this Section) are increased, decreased, or exchanged for a different number or kind of shares or

other securities, or if additional shares or new or different shares or other securities are distributed with respect to Shares, as a result of a reorganization, recapitalization, reclassification, stock dividend, stock split, reverse stock split, or other similar distribution with respect to such Shares, an appropriate and proportionate adjustment will be made in (i) the maximum numbers and kinds of shares provided in Section 3, (ii) the numbers and kinds of shares or other securities subject to the then outstanding options, and (iii) the exercise price for each share or other unit of any other securities subject to then outstanding options.

12.2. Adjustment Upon the Occurrence of Certain Unusual or Nonrecurring Events. In the event of any corporate action not specifically covered by the preceding Section 12.1, including but not limited to an extraordinary cash distribution on Common Stock, a corporate separation or other reorganization or liquidation, the Committee may make such adjustment of outstanding options and their terms, if any, as it, in its sole discretion, may deem equitable and appropriate in the circumstances. The Committee may make adjustments in the terms and conditions of, and the criteria included in, options in recognition of unusual or nonrecurring events (including, without limitation, the events described in this Section 12.2) affecting the Company or the financial statements of the Company or of changes in applicable laws, regulations, or accounting principles, whenever the Committee determines that such adjustments are appropriate in order to prevent dilution or enlargement of the benefits or potential benefits intended to be made available under the Plan.

12.3. Related Matters. Any adjustment in options made pursuant to Section 12.1 or 12.2 shall be determined and made, if at all, by the Committee, acting in its sole discretion, and shall include any correlative modification of terms which the Committee may deem necessary or appropriate so as to ensure the rights of the Participating Employees in their respective options are not substantially diminished nor enlarged as a result of the adjustment and corporate action other than as expressly contemplated in this Section 12.

12.4. Corporate Transactions. In the event of a Corporate Transaction that is a dissolution or liquidation of the Company, the Plan Period then in progress will terminate immediately prior to the consummation of such action, unless otherwise provided by the Committee. In the event of any other Corporate Transaction, each option outstanding under the Plan may be assumed or an equivalent option may be substituted by the successor corporation or a parent or subsidiary of such successor corporation. In the event that the successor corporation refuses to assume or substitute for outstanding options, the Plan Period then in progress shall be shortened and a new Plan Period Termination Date shall be set (the "New Plan Period Termination Date"), as of which date the Plan Period then in progress will terminate. The New Plan Period Termination Date shall be on or before the date of consummation of the Corporate Transaction and the Committee shall notify each Participating Employee in writing, at least three Business Days prior to the New Plan Period Termination Date, that the Plan Period Termination Date for his or her option has been changed to the New Plan Period Termination Date and that his or her option will be exercised automatically on the New Plan Period Termination Date, unless prior to such date he or she has withdrawn from the Plan Period as provided in Section 6.7. For purposes of this Section 12.4, an option granted under the Plan shall be considered assumed, or a substantially equivalent award shall be considered to have been provided in substitution therefor, if following consummation of the Corporate Transaction, the option is assumed and/or exchanged or replaced with another option issued by the acquiring or succeeding entity (or an affiliate thereof) that confers the right to receive upon exercise of such option, for each share of Common Stock subject to the option immediately prior to the consummation of the Corporate Transaction, the consideration (whether cash, securities or other property) received as a result of the Corporate

Transaction by holders of Common Stock for each share of Common Stock held immediately prior to the consummation of the Corporate Transaction (and if holders were offered a choice of consideration, the type of consideration chosen by the holders of a majority of the outstanding shares of Stock); *provided however* that if the consideration received in the transaction is not solely common stock of the successor corporation or its parent (as defined in Section 424(e) of the Code), the Committee may, with the consent of the successor corporation, provide for the consideration to be received upon exercise of the option to be solely common stock of the successor corporation or its parent equal in fair market value to the per Share consideration received by holders of Common Stock in the transaction.

**13. Settlement of Awards**

13.1. Violation of Law. Notwithstanding any other provision of the Plan to the contrary, if, at any time, in the reasonable opinion of the Company, the issuance of Shares pursuant to the Plan may constitute a violation of law, then the Company may delay such issuance of such Shares until (i) approval shall have been obtained from such governmental agencies, other than the Commission, as may be required under any applicable law, rule, or regulation and (ii) in the case where such issuance would constitute a violation of a law administered by or a regulation of the Commission, one of the following conditions shall have been satisfied:

(a) the Shares are, at the time of the issue of such Shares, effectively registered under the Securities Act; or

(b) the Company shall have determined, on such basis as it deems appropriate (including an opinion of counsel in form and substance satisfactory to the Company) that the sale, transfer, assignment, pledge, encumbrance or other disposition of such Shares or such beneficial interest, as the case may be, does not require registration under the Securities Act or any applicable state securities laws.

The Company shall make all reasonable efforts to bring about the occurrence of said events.

13.2. Corporate Restrictions on Rights in Stock. Any Shares to be issued pursuant to the Plan shall be subject to all restrictions upon the transfer thereof which may be now or hereafter imposed by the certificate of incorporation and bylaws of the Company.

13.3. Investment Representations. As a condition to the exercise of an option, the Company may require the person exercising such option to represent and warrant at the time of any such exercise that the Shares are being purchased only for investment and without any present intention to sell or distribute such Shares if, in the opinion of counsel for the Company, such a representation is required by any of the aforementioned applicable provisions of law. The Company shall be under no obligation to issue any Shares unless the Shares to be issued pursuant to the Plan have been effectively registered under the Securities Act.

13.4. Placement of Legends; Stop Orders; etc. Each Share to be issued pursuant to the Plan may bear a reference to any applicable restriction under the Plan. All Shares or other securities delivered under the Plan shall be subject to such stop transfer orders and other restrictions as the Committee may deem advisable under the rules, regulations, and other requirements of any stock exchange upon which the Common Stock is then listed, and any applicable federal or state securities law, and the Committee may cause a legend or legends to be put on any such certificates to make appropriate reference to such restrictions.

13.5. Company Charter and By-Laws; Other Company Policies. This Plan and all options granted under this Plan (including the exercise of an option) are subject to and must comply with the certificate of incorporation and bylaws of the Company, as they may be amended from time to time, and all other Company policies duly adopted by the Board, the Committee or any other committee of the Board as in effect from time to time regarding the acquisition, ownership or sale of Common Stock by employees, including, without limitation, policies intended to limit the potential for insider trading and to avoid or recover compensation payable or paid on the basis of inaccurate financial results or statements, employee conduct, and other similar events.

**14. Adopting Subsidiaries**

Any Subsidiary of the Company may request that its Employees be allowed to participate in the Plan in accordance with procedures to be adopted by the Board. The Board may, in its sole discretion, approve or reject any such request. Any such Subsidiary whose request is approved by the Board shall be referred to herein as a "Covered Entity." In addition, the Board may determine, in its sole discretion, that a Subsidiary that is a Covered Entity will cease to be a Covered Entity with respect to Plan Periods not yet commenced.

**15. Amendment and Termination**

(a) The Committee may at any time terminate the Plan or make such modifications of the Plan as it shall deem advisable. Except as provided in Section 12, no termination of the Plan may affect outstanding options, provided that the Plan or a Plan Period may be terminated by the Committee on a Plan Period Termination Date or by the Committee's setting a new Plan Period Termination Date with respect to a Plan Period then in progress if the Committee determines that termination of the Plan and/or any Plan Period is in the best interests of the Company and its stockholders or if continuation of the Plan and/or a Plan Period would cause the Company to incur adverse accounting charges as a result of the Plan. Except as provided in Section 12 or this Section 15, no amendment to the Plan shall make any change in any outstanding option which adversely affects the rights of any Participating Employee.

(b) In addition to the foregoing, without stockholder consent and without regard to whether any Participating Employee rights may be considered to have been adversely affected, the Committee shall be entitled to change the Plan Periods, establish the exchange ratio applicable to amounts withheld in a currency other than U.S. dollars (if applicable), permit payroll withholding in excess of the amount designated by a Participating Employee to adjust for delays or mistakes in the Company's processing of properly completed withholding elections, establish reasonable waiting and adjustment periods and/or accounting and crediting procedures to ensure that amounts applied toward the purchase of Common Stock for each Participating Employee properly correspond with amounts withheld from the Participating Employee's Compensation, and establish such other limitations or procedures as the Committee determines in its sole discretion advisable which are consistent with the Plan.

**16. Notices and Other Communications**

Any notice, demand, request or other communication hereunder to any party shall be deemed to be sufficient if contained in a written instrument delivered in person or duly sent by first class registered, certified or overnight mail, postage prepaid, or by facsimile with a confirmation copy by regular, certified or overnight mail, addressed or by facsimile, as the case may be, (i) if to

a Participating Employee, at his or her residence address last filed with the Company and (ii) if to the Company, at its principal place of business, addressed to the attention of its Chief Financial Officer, or to such other address or facsimile number, as the case may be, as the addressee may have designated by notice to the addressor. All such notices, requests, demands and other communications shall be deemed to have been received: (i) in the case of personal delivery, on the date of such delivery; (ii) in the case of mailing, when received by the addressee; and (iii) in the case of facsimile transmission, when confirmed by facsimile machine report. In addition, the Company may, in its sole discretion, deliver any documents related to the Plan by electronic means or request that the Participating Employee communicate with the Company with respect to the Plan by electronic means. By participating in the Plan, each Participating Employee will have consented to receive such documents by electronic delivery and, if requested, to agree to participate in the Plan through an on-line or electronic system established and maintained by the Company or another third party designated by the Company, and such consent shall remain in effect throughout the Participating Employee's term of employment or service with the Company and thereafter until withdrawn in writing by the Participant.

**17. Governing Law**

The Plan and all options and actions taken thereunder shall be governed, interpreted and enforced in accordance with the laws of the State of Delaware without regard to the conflict of laws principles thereof.

**18. Term of Plan**

The Plan shall become effective on the IPO Date and shall continue in effect until the tenth (10th) anniversary thereof, unless earlier terminated pursuant to Section 15.

*[End of document.]*

**SAMPLE**

**RHYTHM PHARMACEUTICALS, INC.**

**2017 EMPLOYEE STOCK PURCHASE PLAN**

**ENROLLMENT AGREEMENT**

_____ Original Application  Enrollment Date: _____
_____ Change in Payroll Deduction Rate
_____ Change in Beneficiary(ies)

1. I, _____, hereby elect to participate in the Rhythm Pharmaceuticals, Inc. 2017 Employee Stock Purchase Plan (the "Purchase Plan"), and subscribe to purchase shares of the Company's Common Stock in accordance with this Enrollment Agreement and the Purchase Plan. Capitalized terms used (and not otherwise defined) in this enrollment agreement have the meanings assigned to them in the Purchase Plan.

2. I hereby authorize payroll deductions from each paycheck in the amount of _____% of my Compensation (from 1% to 15%) on each payroll date during the Plan Period in accordance with the Purchase Plan. (Please note that no fractional percentages are permitted.)

3. I understand that such payroll deductions will be accumulated for the purchase of shares of Common Stock at the applicable purchase price determined in accordance with the Purchase Plan. I understand that, if I do not withdraw from a Plan Period, any accumulated payroll deductions will be used to automatically purchase shares of Common Stock.

4. I understand that all my payroll deductions received or held by the Company under the Purchase Plan may be used by the Company for any corporate purpose, and the Company shall not be obligated to segregate such payroll deductions. Until shares are issued to me, I will only have the rights of an unsecured creditor with respect to such accumulated payroll deductions.

5. I have received a copy of the Purchase Plan Prospectus and the Purchase Plan document. I understand that my participation in the Purchase Plan is in all respects subject to the terms of the Purchase Plan.

6. Shares purchased for me under the Purchase Plan should be issued in the name(s) of (Employee or Employee and spouse only):

_____

7. I understand that if I dispose of any shares received by me pursuant to the Purchase Plan within two years after the Plan Period Commencement Date (the first day of a Plan Period during which I purchased such shares) or one year after the Plan Period Termination Date, I will be treated for federal income tax purposes as having received ordinary income at the time of such disposition in an amount equal to the excess of the fair market value of the shares at the time such shares were purchased by me over the price which I paid for the shares. **I hereby agree to notify the Company in writing within five (5) business days after the date of any disposition of my shares, and I will make adequate provision for federal, state or other tax withholding obligations, if any, which arise upon the disposition of the Common Stock**. The Company may, but will not be obligated to, withhold from my compensation the amount necessary to meet any applicable withholding obligation, including any withholding necessary to make available to the Company any tax deductions or benefits attributable to the sale or early disposition of Common Stock by me.

If I dispose of such shares at any time after the expiration of the applicable holding periods, I understand that I will be treated for federal income tax purposes as having received income only at the time of such disposition, and that such income will be taxed as ordinary income only to the extent of an amount equal to the lesser of (a) the excess of the fair market value of the shares at the time of such disposition over the purchase price which I paid for the shares or (b) 15% of the fair market value of the shares on the first day of the Plan Period. The remainder of the gain, if any, recognized on such disposition will be taxed as capital gain.

8. I hereby agree to be bound by the terms of the Purchase Plan. The effectiveness of this Enrollment Agreement is dependent upon my eligibility to participate in the Purchase Plan.

[9. I hereby agree to establish a brokerage account with _____ and to fill out and submit the necessary forms to allow the Company to deposit shares purchased on my behalf under the Purchase Plan in such account, if I have not done so already.]

10. In the event of my death, I hereby designate the following as my beneficiary(ies) to receive all payments and shares due me under the Purchase Plan:

BENEFICIARY NAME: (Please print) _____
(First) (Middle) (Last)

_____
Relationship

I UNDERSTAND THAT THIS ENROLLMENT AGREEMENT SHALL REMAIN IN EFFECT THROUGHOUT SUCCESSIVE PLAN PERIODS UNLESS TERMINATED BY ME.

Dated: _____

_____
Signature of Employee

_____
Print name

_____
Spouse's Signature
(If beneficiary other than spouse)

**SAMPLE**

**RHYTHM PHARMACEUTICALS, INC.**

**2017 EMPLOYEE STOCK PURCHASE PLAN**

**NOTICE OF WITHDRAWAL**

The undersigned participant in the Rhythm Pharmaceuticals, Inc. 2017 Employee Stock Purchase Plan, hereby notifies the Company that he or she hereby withdraws from the Plan Period beginning _____. He or she hereby directs the Company to pay to the undersigned as promptly as practicable all the payroll deductions credited to his or her account with respect to such Plan Period. The undersigned understands and agrees that his or her option for such Plan Period will be automatically terminated, that no further payroll deductions will be made for the purchase of shares in the current Plan Period, and that the undersigned shall be eligible to participate in subsequent Plan Periods only by delivering to the Company a new Enrollment Agreement.

Name: _____

Signature: _____

Date: _____

**Exhibit 10.2**

# RHYTHM PHARMACEUTICALS, INC.

# 2017 EQUITY INCENTIVE PLAN

**Table Of Contents**

**Rhythm Pharmaceuticals, Inc.**

**2017 Equity Incentive Plan**

## 1. Purpose

This Plan is intended to provide incentives that will attract, retain and motivate highly competent officers, directors, employees, consultants and advisors to promote the success of the Company's business and align employees' interests with stockholders' interests. The Plan is intended to be an incentive stock option plan within the meaning of Section 422 of the Code, but not all Awards are required to be Incentive Options.

This Plan serves as the successor to the Company's 2015 Equity Incentive Plan (the "Predecessor Plan"), and no further awards shall be made under the Predecessor Plan on or after the Effective Date. All awards outstanding under the Predecessor Plan on the Effective Date shall be transferred to this Plan and shall be treated as outstanding under this Plan. However, each outstanding award so transferred shall continue to be governed solely by the terms of the documents evidence such award, and no provision of the Plan shall be deemed to affect or modified the rights or obligations of the holders of such transferred awards. This Plan and all definitions hereunder shall be interpreted consistent with the foregoing.

## 2. Definitions

As used in this Plan, the following terms shall have the respective meanings set out below, unless the context clearly requires otherwise:

2.1. Accelerate, Accelerated, and Acceleration, means: (a) when used with respect to an Option or Stock Appreciation Right, that as of the time of reference such Option or Stock Appreciation Right will become exercisable with respect to some or all of the shares of Stock for which it was not then otherwise exercisable by its terms; (b) when used with respect to Restricted Stock or Restricted Stock Units, that the Risk of Forfeiture otherwise applicable to such Restricted Stock or Restricted Stock Units shall expire with respect to some or all of such shares of Restricted Stock or such Restricted Stock Units then still otherwise subject to the Risk of Forfeiture; and (c) when used with respect to Performance Units, that the applicable Performance Goals or other business objectives shall be deemed to have been met as to some or all of such Performance Units.

2.2. Affiliate means any parent or subsidiary corporation of the Company (within the meaning of Sections 424(e) and 424(f) of the Code, respectively).

2.3. Award means any grant or sale pursuant to the Plan or award outstanding under the Predecessor Plan as of the Effective Date of Options, Stock Appreciation Rights, Performance Units, Restricted Stock, Restricted Stock Units, Stock Grants or any of the foregoing intended to constitute Qualified Performance-Based Awards.

2.4. Award Agreement means an agreement between the Company and the recipient of an Award, or other notice of grant of an Award, setting forth the terms and conditions of the Award.

2.5. Board means the Company's Board of Directors.

2.6. Change of Control means the occurrence of any of the following after the date of the approval of the Plan by the Board:

(a) a Transaction (as defined in Section 8.4), unless securities possessing more than 50% of the total combined voting power of the survivor's or acquiror's outstanding securities (or the securities of any parent thereof) are held by a person or persons who held securities possessing more than 50% of the total combined voting power of the Company's outstanding securities immediately prior to that Transaction; or

(b) any person or group of persons (within the meaning of Section 13(d)(3) of the Securities Exchange Act of 1934, as amended and in effect from time to time) that, directly or indirectly, acquires, including but not limited to by means of a merger or consolidation, beneficial ownership (determined pursuant to Securities and Exchange Commission Rule 13d-3 promulgated under the said Exchange Act) of securities possessing more than 50% of the total combined voting power of the Company's outstanding securities unless pursuant to a tender or exchange offer made directly to the Company's stockholders that the Board recommends such stockholders accept, other than (i) the Company or any of its Affiliates, (ii) an employee benefit plan of the Company or any of its Affiliates, (iii) a trustee or other fiduciary holding securities under an employee benefit plan of the Company or any of its Affiliates, or (iv) an underwriter temporarily holding securities pursuant to an offering of such securities; or

(c) over a period of thirty-six (36) consecutive months or less, there is a change in the composition of the Board such that a majority of the Board members (rounded up to the next whole number, if a fraction) ceases, by reason of one or more proxy contests for the election of Board members, to be composed of individuals who either (i) have been Board members continuously since the beginning of that period, or (ii) have been elected or nominated for election as Board members during such period by at least a majority of the Board members described in the preceding clause (i) who were still in office at the time that election or nomination was approved by the Board; or

(d) a majority of the Board votes in favor of a decision that a Change of Control has occurred, which vote may adopted by the Board with the intention that such vote become effective subject to and contingent upon the occurrence of certain events, in which case such Change of Control shall not be deemed to have occurred unless and until such vote becomes effective in accordance with its terms.

2.7. Code means the Internal Revenue Code of 1986, as amended from time to time, or any successor statute thereto, and any regulations issued from time to time thereunder.

2.8. Committee means the Compensation Committee of the Board, which in general is responsible for the administration of the Plan, as provided in Section 5 of this Plan. For any period during which no such committee is in existence "Committee" shall mean the Board and all authority and responsibility assigned to the Committee under the Plan shall be exercised, if at all, by the Board.

2.9. Company means Rhythm Pharmaceuticals, Inc., a corporation organized under the laws of the State of Delaware.

2.10. "Forfeiture," "forfeit," and derivations thereof, when used in respect of Restricted Stock purchased by a Participant, includes the Company's repurchase of such Restricted Stock at less than its then Market Value as a means intended to effect a forfeiture of value.

2.11. Grant Date means the date as of which an Option is granted, as determined under Section 7.1(a).

2.12. Incentive Option means an Option which by its terms is to be treated as an "incentive stock option" within the meaning of Section 422 of the Code.

2.13. Market Value means the value of a share of Stock on a particular date determined by such methods or procedures as may be established by the Committee. Unless otherwise determined by the Committee, the Market Value of Stock as of any date is the closing price for the Stock as reported on the Nasdaq Stock Market (or on any other national securities exchange on which the Stock is then listed) for that date or, if no closing price is reported for that date, the closing price on the first following date for which a closing price is reported. For purposes of Awards effective as of the effective date of the Company's initial public offering, Market Value of Stock shall be the price at which the Company's Stock is offered to the public in its initial public offering.

2.14. Nonstatutory Option means any Option that is not an Incentive Option.

2.15. Option means an option to purchase shares of Stock.

2.16. Optionee means an eligible individual to whom an Option shall have been granted under the Plan.

2.17. Participant means any holder of an outstanding Award under the Plan or the Predecessor Plan.

2.18. Performance Criteria and Performance Goals have the meanings given such terms in Section 7.7(f).

2.19. Performance Period means one or more periods of time, which may be of varying and overlapping durations, selected by the Committee, over which the attainment of one or more Performance Goals or other business objectives will be measured for purposes of determining a Participant's right to, and the payment of, an Award.

2.20. Performance Unit means a right granted to a Participant under Section 7.5, to receive cash, Stock or other Awards, the payment of which is contingent on achieving Performance Goals or other business objectives established by the Committee.

2.21. Plan means this 2017 Equity Incentive Plan of the Company, as amended from time to time, and including any attachments or addenda hereto.

2.22. Qualified Performance-Based Awards means Awards intended to qualify as "performance-based compensation" under Section 162(m) of the Code.

2.23. Restricted Stock means a grant or sale of shares of Stock to a Participant subject to a Risk of Forfeiture.

2.24. Restricted Stock Units means rights to receive shares of Stock, cash or other Awards at the close of a Restriction Period, subject to a Risk of Forfeiture.

2.25. Restriction Period means the period of time, established by the Committee in connection with an Award of Restricted Stock or Restricted Stock Units, during which the shares of Restricted Stock or Restricted Stock Units are subject to a Risk of Forfeiture described in the applicable Award Agreement.

2.26. Risk of Forfeiture means a limitation on the right of the Participant to retain Restricted Stock or Restricted Stock Units, including a right of the Company to reacquire shares of Restricted Stock at less than their then Market Value, arising because of the occurrence or non-occurrence of specified events or conditions.

2.27. Stock means common stock, par value $0.001 per share, of the Company, and such other securities as may be substituted for such common stock pursuant to Section 8.

2.28. Stock Appreciation Right means a right to receive any excess in the Market Value of shares of Stock (except as otherwise provided in Section 7.2(c)) over a specified exercise price.

2.29. Stock Grant means the grant of shares of Stock not subject to restrictions or other forfeiture conditions.

2.30. Stockholders' Agreement means any agreement by and among the holders of at least a majority of the outstanding voting securities of the Company and setting forth, among other provisions, restrictions upon the transfer of shares of Stock or on the exercise of rights appurtenant thereto (including but not limited to voting rights).

2.31. Ten Percent Owner means a person who owns, or is deemed within the meaning of Section 422(b)(6) of the Code to own, stock possessing more than 10% of the total combined voting power of all classes of stock of the Company (or any parent or subsidiary corporations of the Company, as defined in Sections 424(e) and (f), respectively, of the Code). Whether a person is a Ten Percent Owner shall be determined with respect to an Option based on the facts existing immediately prior to the Grant Date of the Option.

**3. Term of the Plan**

The Plan became effective on October 10, 2017 upon consummation of the Company's initial public offering (the "Effective Date") and, unless earlier terminated by the Committee, shall terminate on October 10, 2027. Awards granted pursuant to the Predecessor Plan or to the Plan within that period shall not expire solely by reason of the termination of the Plan.

**4. Stock Subject to the Plan**

4.1. Plan Share Limitations.

(a) Limitation. The maximum number of shares of Stock that may be issued pursuant to or subject to outstanding Awards granted under the Plan shall not exceed 4,018,538 shares of Stock. Such share reserve includes 1,821,580 shares of Stock available for issuance under the Predecessor Plan as of the Effective Date, including the portion of those shares subject to Options outstanding under the Predecessor Plan as of the Effective Date, plus an additional 2,196,958 shares. Notwithstanding the foregoing, however, beginning on the first January 1 following consummation of the Company's initial public offering, the number of shares of Stock authorized under the first sentence of this Section 4.1(a) of the Plan will be increased each January 1 by an amount equal to four percent (4%) of outstanding shares of Stock as of the end of the immediately preceding fiscal year. Notwithstanding the foregoing, the Board may act prior to January 1 of a given year to provide that there will be no such January 1 increase in the number of shares of Stock authorized under this Section 4.1(a) of the Plan for such year or that the increase in the number of shares of Stock authorized under this Section 4.1(a) of the Plan for such year will be a lesser number than would otherwise occur pursuant to the preceding sentence. Notwithstanding the preceding sentences, in no

event shall the number of shares available for issuance pursuant to Incentive Options over the term of the Plan exceed 4,018,538 shares of Stock.

(b) Application. For purposes of applying the foregoing limitation of Section 4.1(a), (i) if any Option or Stock Appreciation Right expires, terminates, or is cancelled for any reason without having been exercised in full, or if any other Award is forfeited, the shares of Stock not purchased by the holder or subject to Awards which are forfeited, as the case may be, shall again be available for Awards to be granted under the Plan, (ii) if any Option is exercised by delivering previously owned shares of Stock or the withholding of a portion of the otherwise issuable shares of Stock subject to the Option in payment of the exercise price therefor, only the net number of shares, that is, the number of shares of Stock issued minus the number received by the Company in payment of the exercise price, shall be considered to have been issued pursuant to an Award granted under the Plan, and (iii) any shares of Stock either delivered to or withheld by the Company in satisfaction of tax withholding obligations of the Company or an Affiliate with respect to an Award shall again be available for Awards to be granted under the Plan. In addition, settlement of any Award shall not count against the foregoing limitations except to the extent settled in the form of Stock. For the avoidance of doubt, Awards outstanding under the Predecessor Plan shall be treated consistent with Awards granted under this Plan for all purposes, including for purposes of this Section 4.1(b). Shares of Stock issued pursuant to the Plan may be either authorized but unissued shares or shares held by the Company in its treasury.

4.2. Per Person Limitations. The maximum number of shares of Stock that may be subject to Options or Stock Appreciation Rights or any combination thereof granted to any one Participant during any single calendar year shall be 1,200,000. The maximum number of shares of Stock that may be subject to all other Awards or any combination thereof granted to any one Participant during any single calendar year that are intended to be Qualified Performance-Based Awards shall be 1,200,000. The maximum value of awards denominated in cash granted to any one person, other than a non-employee member of the Board, during any single calendar year and that are intended to be Qualified Performance-Based Awards shall be $30,000,000. Each of the foregoing limitations shall be doubled with respect to awards granted to an individual during the first calendar year in which he or she commences employment. The per Participant limits described in this Section 4.2 shall be construed and applied consistent with Section 162(m) of the Code.

4.3. Limitations on Grants to Non-Employee Board Members. The maximum value of awards denominated in cash granted to any non-employee member of the Board, during any single calendar year shall be $1,000,000. For purposes of this limitation, the value of an award shall be the grant date fair value of the award (as determined for the Company's financial statements).

4.4. Adjustment of Limitations. Each of the share limitations of this Section 4 shall be subject to adjustment pursuant to Section 8 of the Plan, but in the case of the limitations of Section 4.2, only if and to the extent consistent with Section 162(m) of the Code.

**5. Administration**

The Plan shall be administered by the Committee; provided, however, that at any time and on any one or more occasions the Board may itself exercise any of the powers and responsibilities assigned the Committee under the Plan and when so acting shall have the benefit of all of the provisions of the Plan pertaining to the Committee's exercise of its authorities hereunder; and provided further, however, that the Committee may delegate to an executive officer or officers the authority to grant Awards hereunder to employees who are not executive officers, and to consultants, up to such maximum number and in accordance with such other guidelines as the Committee shall specify by resolution at any time or from time to time. To the extent required by applicable law, any such delegation may not include the authority

to grant Restricted Stock, unless the delegate is a committee of the Board, including a committee consisting solely of an executive officer who is a Board member. Subject to the provisions of the Plan, the Committee shall have complete authority, in its discretion, to make or to select the manner of making all determinations with respect to each Award to be granted by the Company under the Plan including the officer, employee, consultant, advisor or director to receive the Award and the form of Award. In making such determinations, the Committee may take into account the nature of the services rendered by the respective officers, employees, consultants, advisors and directors, their present and potential contributions to the success of the Company and its Affiliates, and such other factors as the Committee in its discretion shall deem relevant. Subject to the provisions of the Plan, the Committee shall also have complete authority to interpret the Plan, to prescribe, amend and rescind rules and regulations relating to it, to determine the terms and provisions of the respective Award Agreements (which need not be identical), and to make all other determinations necessary or advisable for the administration of the Plan. The Committee's determinations made in good faith on matters referred to in the Plan shall be final, binding and conclusive on all participants, beneficiaries, heirs, assigns or other persons having or claiming any interest under the Plan or an Award made pursuant hereto.

**6. Authorization of Grants**

6.1. Eligibility. The Committee may grant from time to time and at any time prior to the termination of the Plan one or more Awards, either alone or in combination with any other Awards, to any officer or employee of or consultant or advisor to one or more of the Company and its Affiliates or to any non-employee member of the Board or of any board of directors (or similar governing authority) of any Affiliate. However, only employees of the Company and its Affiliates shall be eligible for the grant of an Incentive Option.

6.2. General Terms of Awards. Each grant of an Award shall be subject to all applicable terms and conditions of the Plan (including but not limited to any specific terms and conditions applicable to that type of Award set out in the following Section), and such other terms and conditions, not inconsistent with the terms of the Plan, as the Committee may prescribe. No prospective Participant shall have any rights with respect to an Award, unless and until such Participant shall have complied with the applicable terms and conditions of such Award (including if applicable delivering a fully executed copy of any agreement evidencing an Award to the Company).

6.3. Effect of Termination of Employment, Etc. Unless the Committee shall provide otherwise with respect to any Award (including, but not limited to, in a Participant's Award Agreement), if the Participant's employment or other association with the Company and its Affiliates ends for any reason, including because of the Participant's employer ceasing to be an Affiliate, (a) any outstanding Option or Stock Appreciation Right of the Participant shall cease to be exercisable in any respect not later than ninety (90) days following that event and, for the period it remains exercisable following that event, shall be exercisable only to the extent exercisable at the date of that event, and (b) any other outstanding Award of the Participant to the extent that it is then still subject to Risk of Forfeiture shall be forfeited or otherwise subject to return to or repurchase by the Company on the terms specified in the applicable Award Agreement. Cessation of the performance of services in one capacity, for example, as an employee, shall not result in termination of an Award while the Participant continues to perform services in another capacity, for example as a director. Military or sick leave or other bona fide leave approved by the Company shall not be deemed a termination of employment or other association; *provided*, however, that should such leave exceed three (3) months, then for purposes of determining the period within which an Incentive Option may be exercised as such under the federal tax laws, the Participant's service shall be deemed to cease on the first day immediately following the expiration of such three (3)-month period, unless the Participant is provided with the right to return to employment following such leave either by statute or by written contract.. To the extent consistent with applicable law, the Committee may provide that Awards

continue to vest for some or all of the period of any such leave, or that their vesting shall be tolled during any such leave and only recommence upon the Participant's return from leave, if ever.

6.4. Non-Transferability of Awards. Except as otherwise provided in this Section 6.4, Awards shall not be transferable, and no Award or interest therein may be sold, transferred, pledged, assigned, or otherwise alienated or hypothecated, other than by will or by the laws of descent and distribution. The provisions of the immediately preceding sentence shall not be applicable to Stock Grants which shall not be subject to any transfer restrictions under this Section 6.4. All of a Participant's rights in any Award may be exercised during the life of the Participant only by the Participant or the Participant's legal representative. However, the Committee may, at or after the grant of an Award of a Nonstatutory Option, or shares of Restricted Stock, provide that such Award may be transferred by the recipient to a family member; *provided, however*, that any such transfer is without payment of any consideration whatsoever and that no transfer shall be valid unless first approved by the Committee, acting in its sole discretion. For this purpose, "family member" means any child, stepchild, grandchild, parent, grandparent, stepparent, spouse, former spouse, sibling, niece, nephew, mother-in-law, father-in-law, son-in-law, daughter-in-law, brother-in-law, or sister-in-law, including adoptive relationships, any person sharing the employee's household (other than a tenant or employee), a trust in which the foregoing persons have more than fifty (50) percent of the beneficial interests, a foundation in which the foregoing persons (or the Participant) control the management of assets, and any other entity in which these persons (or the Participant) own more than fifty (50) percent of the voting interests.

**7. Specific Terms of Awards**

7.1. Options.

(a) Date of Grant. The granting of an Option shall take place at the time specified in the Award Agreement.

(b) Exercise Price. The price at which shares of Stock may be acquired under each Option shall be not less than 100% of the Market Value of Stock on the Grant Date, or for an Incentive Option not less than 110% of the Market Value of Stock on the Grant Date if the Optionee is a Ten Percent Owner.

(c) Option Period. No Incentive Option may be exercised on or after the tenth (10th) anniversary of the Grant Date, or on or after the fifth (5th) anniversary of the Grant Date if the Optionee is a Ten Percent Owner. The Option period under each Nonstatutory Option shall not be so limited solely by reason of this Section.

(d) Exercisability. An Option may be immediately exercisable or become exercisable in such installments, cumulative or non-cumulative, as the Committee may determine. In the case of an Option not otherwise immediately exercisable in full, the Committee may Accelerate such Option in whole or in part at any time; *provided, however,* that in the case of an Incentive Option, any such Acceleration of the Option would not cause the Option to fail to comply with the provisions of Section 422 of the Code or the Optionee consents to the Acceleration.

(e) Method of Exercise. An Option may be exercised by the Optionee giving written notice, in the manner provided in Section 17, specifying the number of shares of Stock with respect to which the Option is then being exercised. The notice shall be accompanied by payment in the form of cash or check payable to the order of the Company in an amount equal to the exercise price of the shares of Stock to be purchased or, subject in each instance to the Committee's approval, acting in its sole discretion, and

to such conditions, if any, as the Committee may deem necessary to avoid adverse accounting effects to the Company,

(i) by delivery to the Company of shares of Stock having a Market Value equal to the exercise price of the shares to be purchased, or

(ii) by the Company withholding shares of Stock otherwise issuable under the Option with such withheld shares having an aggregate Market Value equal to the aggregate exercise price of the shares to be purchased, or

(iii) unless prohibited by applicable law, by delivery to the Company of the Optionee's executed promissory note in the principal amount equal to the exercise price of the shares of Stock to be purchased and otherwise in such form as the Committee shall have approved.

If the Stock is traded on an established market, payment of any exercise price may also be made through and under the terms and conditions of any formal cashless exercise program authorized by the Company entailing the sale of the Stock subject to an Option in a brokered transaction (other than to the Company). Receipt by the Company of such notice and payment in any authorized or combination of authorized means shall constitute the exercise of the Option. Within thirty (30) days thereafter but subject to the remaining provisions of the Plan, the Company shall deliver or cause to be delivered to the Optionee or his agent a certificate or certificates or shall cause the Stock to be held in book-entry position through the direct registration system of the Company's transfer agent for the number of shares then being purchased. Such shares of Stock shall be fully paid and nonassessable.

(f) Limit on Incentive Option Characterization. An Incentive Option shall be considered to be an Incentive Option only to the extent that the number of shares of Stock for which the Option first becomes exercisable in a calendar year do not have an aggregate Market Value (as of the date of the grant of the Option) in excess of the "current limit". Except to the extent otherwise provided under applicable law or regulation, the current limit for any Optionee for any calendar year shall be $100,000 *minus* the aggregate Market Value at the date of grant of the number of shares of Stock available for purchase for the first time in the same year under each other Incentive Option previously granted to the Optionee under the Plan, and under each other incentive stock option previously granted to the Optionee under any other incentive stock option plan of the Company and its parent and subsidiary corporations (as defined in Sections 424(e) and (f) of the Code). Any shares of Stock which would cause the foregoing limit to be violated shall be deemed to have been granted under a separate Nonstatutory Option, otherwise identical in its terms to those of the Incentive Option.

(g) Notification of Disposition. Each person exercising any Incentive Option granted under the Plan shall be deemed to have covenanted with the Company to report to the Company any disposition of the shares of Stock issued upon such exercise prior to the expiration of the holding periods specified by Section 422(a)(1) of the Code and, if and to the extent that the realization of income in such a disposition imposes upon the Company federal, state, local or other withholding tax requirements, or any such withholding is required to secure for the Company an otherwise available tax deduction, to remit to the Company an amount in cash sufficient to satisfy those requirements.

7.2. Stock Appreciation Rights.

(a) Tandem or Stand-Alone. Stock Appreciation Rights may be granted in tandem with an Option (at or, in the case of a Nonstatutory Option, after, the award of the Option), or alone and unrelated to an Option. Stock Appreciation Rights in tandem with an Option shall terminate to the extent

that the related Option is exercised, and the related Option shall terminate to the extent that the tandem Stock Appreciation Rights are exercised.

(b) Exercise Price. Stock Appreciation Rights shall have an exercise price of not less than one hundred percent (100%) of the Market Value of the Stock on the date of award, or in the case of Stock Appreciation Rights in tandem with Options, the exercise price of the related Option.

(c) Other Terms. Except as the Committee may deem inappropriate or inapplicable in the circumstances, Stock Appreciation Rights shall be subject to terms and conditions substantially similar to those applicable to a Nonstatutory Option. In addition, a Stock Appreciation Right related to an Option which can only be exercised during limited periods following a Change of Control may entitle the Participant to receive an amount based upon the highest price paid or offered for Stock in any transaction relating to the Change of Control or paid during the thirty (30) day period immediately preceding the occurrence of the Change of Control in any transaction reported in the stock market in which the Stock is normally traded.

7.3. Restricted Stock.

(a) Purchase Price. Shares of Restricted Stock shall be issued under the Plan for such consideration, if any, in cash, other property or services, or any combination thereof, as is determined by the Committee.

(b) Issuance of Stock. Each Participant receiving a Restricted Stock Award, subject to subsection (c) below, shall be issued a stock certificate in respect of such shares of Restricted Stock or the shares shall be held in book-entry position through the direct registration system of the Company's transfer agent. If a certificate is issued, such certificate shall be registered in the name of such Participant, and, if applicable, shall bear an appropriate legend referring to the terms, conditions, and restrictions applicable to such Award substantially in the following form:

> "The shares evidenced by this certificate are subject to the terms and conditions of Rhythm Pharmaceuticals, Inc.'s 2017 Equity Incentive Plan and an Award Agreement entered into by the registered owner and Rhythm Pharmaceuticals, Inc., copies of which will be furnished by the Company to the holder of the shares evidenced by this certificate upon written request and without charge."

If the Stock is in book-entry position through the direct registration system of the Company's transfer agent, the restrictions will be appropriately noted.

(c) Escrow of Shares. The Committee may require that any stock certificates evidencing shares of Restricted Stock be held in custody by a designated escrow agent (which may but need not be the Company) until the restrictions thereon shall have lapsed, and that the Participant deliver a stock power, endorsed in blank, relating to the Stock covered by such Award.

(d) Restrictions and Restriction Period. During the Restriction Period applicable to shares of Restricted Stock, such shares shall be subject to limitations on transferability and a Risk of Forfeiture arising on the basis of such conditions related to the performance of services, Company or Affiliate performance or otherwise as the Committee may determine and provide for in the applicable Award Agreement. Any such Risk of Forfeiture may be waived or terminated, or the Restriction Period shortened, at any time by the Committee on such basis as it deems appropriate.

(e) Rights Pending Lapse of Risk of Forfeiture or Forfeiture of Award. Except as otherwise provided in the Plan or the applicable Award Agreement, the Participant shall have all of the rights of a stockholder of the Company with respect to any outstanding shares of Restricted Stock, including the right to vote, and the right to receive any dividends with respect to, the shares of Restricted Stock (but any dividends or other distributions payable in shares of Stock or other securities of the Company shall constitute additional Restricted Stock, subject to the same Risk of Forfeiture as the shares of Restricted Stock in respect of which such shares of Stock or other securities are paid). The Committee, as determined at the time of Award, may permit or require the payment of cash dividends to be deferred and, if the Committee so determines, reinvested in additional Restricted Stock to the extent shares of Stock are available under Section 4.

(f) Lapse of Restrictions. If and when the Restriction Period expires without a prior forfeiture, any certificates for such shares shall be delivered to the Participant promptly if not theretofore so delivered.

7.4. Restricted Stock Units.

(a) Character. Subject to Section 10, each Restricted Stock Unit shall entitle the recipient to a share of Stock at a close of such Restriction Period as the Committee may establish and subject to a Risk of Forfeiture arising on the basis of such conditions relating to the performance of services, Company or Affiliate performance or otherwise as the Committee may determine and provide for in the applicable Award Agreement. Any such Risk of Forfeiture may be waived or terminated, or the Restriction Period shortened, at any time by the Committee on such basis as it deems appropriate.

(b) Form and Timing of Payment. Payment of earned Restricted Stock Units shall be made promptly following the close of the applicable Restriction Period. At the discretion of the Committee, Participants may be entitled to receive payments equivalent to any dividends declared with respect to Stock referenced in grants of Restricted Stock Units but only following the close of the applicable Restriction Period and then only if the underlying Stock shall have been earned. Unless the Committee shall provide otherwise, any such dividend equivalents shall be paid, if at all, without interest or other earnings. The Committee may permit or, if it so provides at grant require, a Participant to defer such Participant's receipt of the payment that would otherwise be due to such Participant with respect to Restricted Stock Units. If any such deferral election is required or permitted, the Committee shall establish rules and procedures for such payment deferrals.

7.5. Performance Units.

(a) Character. Each Performance Unit shall entitle the recipient to the value of a specified number of shares of Stock, over the initial value for such number of shares, if any, established by the Committee at the time of grant, at the close of a specified Performance Period to the extent specified business objectives, including but not limited to Performance Goals, shall have been achieved.

(b) Earning of Performance Units. The Committee shall set Performance Goals or other business objectives in its discretion which, depending on the extent to which they are met within the applicable Performance Period, will determine the number and value of Performance Units that will be paid out to the Participant. After the applicable Performance Period has ended, the holder of Performance Units shall be entitled to receive payout on the number and value of Performance Units earned by the Participant over the Performance Period, to be determined as a function of the extent to which the corresponding Performance Goals or other business objectives have been achieved.

(c) Form and Timing of Payment. Unless otherwise provided in the applicable Award Agreement, payment of earned Performance Units shall be made in a single lump sum following the close of the applicable Performance Period. At the discretion of the Committee, Participants may be entitled to receive any dividends declared with respect to Stock which have been earned in connection with grants of Performance Units which have been earned, but not yet distributed to Participants. The Committee may permit or, if it so provides at grant require, a Participant to defer such Participant's receipt of the payment of cash or the delivery of Stock that would otherwise be due to such Participant by virtue of the satisfaction of any requirements or goals with respect to Performance Units. If any such deferral election is required or permitted, the Committee shall establish rules and procedures for such payment deferrals.

7.6. Stock Grants. Stock Grants shall be awarded solely in recognition of significant prior or expected contributions to the success of the Company or its Affiliates, as an inducement to employment, in lieu of compensation otherwise already due and in such other limited circumstances as the Committee deems appropriate. Stock Grants shall be made without forfeiture conditions of any kind.

7.7. Qualified Performance-Based Awards.

(a) Purpose. The purpose of this Section 7.7 is to provide the Committee the ability to qualify Awards as "performance-based compensation" under Section 162(m) of the Code. If the Committee, in its discretion, decides to grant an Award as a Qualified Performance-Based Award, the provisions of this Section 7.7 will control over any contrary provision contained in the Plan. In the course of granting any Award, the Committee may specifically designate the Award as intended to qualify as a Qualified Performance-Based Award. However, no Award shall be considered to have failed to qualify as a Qualified Performance-Based Award solely because the Award is not expressly designated as a Qualified Performance-Based Award, if the Award otherwise satisfies the provisions of this Section 7.7 and the requirements of Section 162(m) of the Code applicable to "performance-based compensation."

(b) Authority. All grants of Awards intended to qualify as Qualified Performance-Based Awards and the determination of the terms applicable thereto shall be made by the Committee. If not all of the members thereof qualify as "outside directors" within the meaning of Section 162 of the Code, however, all grants of Awards intended to qualify as Qualified Performance-Based Awards and the determination of the terms applicable thereto shall be made by a subcommittee of the Committee consisting of such of the members of the Committee as do so qualify. Any reference in this Section 7.7 to the Committee shall mean any such subcommittee if required under the preceding sentence, and any action by such a subcommittee shall be considered the action of the Committee for purposes of the Plan.

(c) Discretion of Committee with Respect to Qualified Performance-Based Awards. Any form of Award permitted under the Plan, other than a Stock Grant, may be granted as a Qualified Performance-Based Award. Options and Stock Appreciation Rights may be granted as Qualified Performance-Based Awards in accordance with Section 7.1 and Section 7.2, respectively, except that the Option or Stock Appreciation Right may become exercisable based on continued service, on satisfaction of Performance Goals or other business objectives, or on a combination thereof. Each other Award intended to qualify as a Qualified Performance-Based Award, such as Restricted Stock, Restricted Stock Units, or Performance Units, shall be subject to satisfaction of one or more Performance Goals except as otherwise provided in this Section 7.7. The Committee will have full discretion to select the length of any applicable Restriction Period or Performance Period, the kind and/or level of the applicable Performance Goal, and whether the Performance Goal is to apply to the Company, a subsidiary of the Company or any division or business unit or to the individual. Any Performance Goal or Goals applicable to Qualified Performance-Based Awards shall be objective, shall be established not later than ninety (90) days after the beginning of any applicable Performance Period (or at such other date as may be required or permitted for "performance-based compensation" under Section 162(m) of the Code) and shall otherwise meet the requirements of

Section 162(m) of the Code, including the requirement that the outcome of the Performance Goal or Goals be substantially uncertain (as defined for purposes of Section 162(m) of the Code) at the time established.

(d) Payment of Qualified Performance-Based Awards. A Participant will be eligible to receive payment under a Qualified Performance-Based Award which is subject to achievement of a Performance Goal or Goals only if the applicable Performance Goal or Goals are achieved within the applicable Performance Period, as determined by the Committee, *provided*, that a Qualified Performance-Based Award may be deemed earned as a result of death, becoming disabled, or in connection with a change of control (within the meaning of Section 162(m) of the Code) if otherwise provided in the Plan or the applicable Award Agreement even if the Award would not constitute "performance-based compensation" under Section 162(m) of the Code following the occurrence of such an event. In determining the actual size of an individual Qualified Performance-Based Award, the Committee may reduce or eliminate the amount of the Qualified Performance-Based Award earned for the Performance Period, if in its sole and absolute discretion, such reduction or elimination is appropriate.

(e) Limitation on Adjustments for Certain Events. No adjustment of any Qualified Performance-Based Award pursuant to Section 8 shall be made except on such basis, if any, as will not cause such Award to provide other than "performance-based compensation" within the meaning of Section 162(m) of the Code.

(f) Definitions. For purposes of the Plan

(i) Performance Criteria means the criteria that the Committee selects for purposes of establishing the Performance Goal or Performance Goals for a Participant for a Performance Period. The Performance Criteria used to establish Performance Goals are limited to: (i) net earnings (either before or after one or more of (A) interest, (B) taxes, (C) depreciation and (D) amortization), (ii) gross or net sales or revenue, (iii) net income (either before or after taxes), (iv) adjusted net income, (v) operating earnings or profit, (vi) cash flow (including, but not limited to, operating cash flow and free cash flow, (vii) return on assets, (viii) return on capital, (ix) return on stockholders' equity, (x) total stockholder return, (xi) return on sales, (xii) gross or net profit or operating margin, (xiii) costs, (xiv) expenses, (xv) working capital, (xvi) earnings per share, (xvii) adjusted earnings per share, (xviii) price per share, (xix) regulatory body approval for commercialization of a product, (xx) implementation, completion or attainment of objectives relating to research, development, regulatory, commercial, or strategic milestones or developments; (xxi) market share, (xxii) economic value, (xxiii) revenue, (xxiv) revenue growth and (xxv) operational and organizational metrics.

(ii) Performance Goals means, for a Performance Period, the written goal or goals established by the Committee for the Performance Period based upon one or more of the Performance Criteria. The Performance Goals may be expressed in terms of overall Company performance or the performance of a division, business unit, subsidiary, or an individual, either individually, alternatively or in any combination, applied to either the Company as a whole or to a business unit or Affiliate, either individually, alternatively or in any combination, and measured either quarterly, annually or cumulatively over a period of years, on an absolute basis or relative to a pre-established target, to previous years' results or to a designated comparison group, in each case as specified by the Committee. The Committee will objectively define the manner of calculating the Performance Goal or Goals it selects to use for such Performance Period for such Participant, including whether or to what extent there shall not be taken into account any of the following events that occurs during a Performance Period: (i) asset write-downs,

(ii) litigation, claims, judgments or settlements, (iii) the effect of changes in tax law, accounting principles or other such laws or provisions affecting reported results, (iv) accruals for reorganization and restructuring programs and (v) any extraordinary, unusual, non-recurring or non-comparable items (A) as described in Accounting Standard Codification Section 225-20, (B) as described in management's discussion and analysis of financial condition and results of operations appearing in the Company's Annual Report to stockholders for the applicable year, or (C) publicly announced by the Company in a press release or conference call relating to the Company's results of operations or financial condition for a completed quarterly or annual fiscal period.

7.8. Awards to Participants Outside the United States. The Committee may modify the terms of any Award under the Plan granted to a Participant who is, at the time of grant or during the term of the Award, resident or primarily employed outside of the United States in any manner deemed by the Committee to be necessary or appropriate in order that the Award shall conform to laws, regulations, procedures, and customs of the country in which the Participant is then resident or primarily employed, or so that the value and other benefits of the Award to the Participant, as affected by foreign tax laws and other restrictions applicable as a result of the Participant's residence or employment abroad, shall be as comparable as practicable to the value of such an Award to a Participant who is resident or primarily employed in the United States. The Committee may establish supplements or sub-plans to, or amendments, restatements, or alternative versions of, the Plan for the purpose of granting and administrating any such modified Award. No such modification, supplement, sub-plan, amendment, restatement or alternative version may increase the share limit of Section 4.

**8. Adjustment Provisions**

8.1. Adjustment for Corporate Actions. All of the share numbers set forth in the Plan reflect the capital structure of the Company as of the Effective Date. If subsequent to that date the outstanding shares of Stock (or any other securities covered by the Plan by reason of the prior application of this Section) are increased, decreased, or exchanged for a different number or kind of shares or other securities, or if additional shares or new or different shares or other securities are distributed with respect to shares of Stock, as a result of a reorganization, recapitalization, reclassification, stock dividend, stock split, reverse stock split, or other similar distribution with respect to such shares of Stock, an equitable adjustment will be made in (i) the maximum numbers and kinds of shares provided in Section 4, (ii) the numbers and kinds of shares or other securities subject to the then outstanding Awards, (iii) the exercise price for each share or other unit of any other securities subject to then outstanding Options and Stock Appreciation Rights (without change in the aggregate purchase price as to which such Options or Rights remain exercisable), and (iv) the repurchase price of each share of Restricted Stock then subject to a Risk of Forfeiture in the form of a Company repurchase right.

8.2. Adjustment of Awards Upon the Occurrence of Certain Unusual or Nonrecurring Events. In the event of any corporate action not specifically covered by the preceding Section, including but not limited to an extraordinary cash distribution on Stock, a corporate separation or other reorganization or liquidation, the Committee shall make such adjustment of outstanding Awards and their terms, if any, as it, in its sole discretion, may deem equitable in the circumstances. The Committee may make adjustments in the terms and conditions of, and the criteria included in, Awards in recognition of unusual or nonrecurring events (including, without limitation, the events described in this Section) affecting the Company or the financial statements of the Company or of changes in applicable laws, regulations, or accounting principles, whenever the Committee determines that such adjustments are appropriate in order to prevent dilution or enlargement of the benefits or potential benefits intended to be made available under the Plan.

8.3. Related Matters. Any adjustment in Awards made pursuant to Section 8.1 or Section 8.2 shall be determined and made, if at all, by the Committee, acting in its sole discretion, and shall include any correlative modification of terms, including of Option exercise prices, rates of vesting or exercisability, Risks of Forfeiture, applicable repurchase prices for Restricted Stock, and Performance Goals and other business objectives which the Committee may deem necessary or appropriate so as to ensure the rights of the Participants in their respective Awards are not substantially diminished nor enlarged as a result of the adjustment and corporate action other than as expressly contemplated in this Section 8. The Committee, in its discretion, may determine that no fraction of a share of Stock shall be purchasable or deliverable upon exercise, and in that event if any adjustment hereunder of the number of shares of Stock covered by an Award would cause such number to include a fraction of a share of Stock, such number of shares of Stock shall be adjusted to the nearest smaller whole number of shares. No adjustment of an Option exercise price per share pursuant to Section 8.1 or Section 8.2 shall result in an exercise price which is less than the par value of the Stock.

8.4. Transactions.

(a) Definition of Transaction. In this Section 8.4, "Transaction" means (1) any merger or consolidation of the Company with or into another entity as a result of which the Stock of the Company is converted into or exchanged for the right to receive cash, securities or other property or is cancelled, (2) any sale or exchange of all or substantially all of the outstanding Stock of the Company for cash, securities or other property, (3) any sale, transfer, or other disposition of all or substantially all of the Company's assets to one or more other persons in a single transaction or series of related transactions or (4) any liquidation or dissolution of the Company.

(b) Treatment of Awards. In a Transaction, the Committee may take any one or more of the following actions as to all or any (or any portion of) outstanding Awards, subject to the provisions of Section 9 of this Plan.

(1) Provide that any Awards shall be assumed, or substantially equivalent rights shall be provided in substitution therefor, by the acquiring or succeeding entity (or an affiliate thereof).

(2) Upon written notice to the holders, provide that all or any of the holders' unexercised outstanding Options and Stock Appreciation Rights (collectively, "Rights") will terminate immediately prior to the consummation of such Transaction unless exercised within a specified period following the date of such notice.

(3) Provide that all or any Awards that are subject to Risk of Forfeiture will terminate immediately prior to the consummation of such Transaction.

(4) Provide that all or any outstanding Rights shall Accelerate so as to become exercisable prior to or upon such Transaction with respect to some or all of the shares of Stock for which any such Rights would not then otherwise be exercisable by their terms.

(5) Provide that all or any outstanding Awards that are subject to Risk of Forfeiture shall Accelerate so that the Risk of Forfeiture otherwise applicable to such Awards shall expire prior to or upon such Transaction with respect to any such Awards that would then still otherwise be subject to the Risk of Forfeiture.

(6) Provide for cash payments, net of applicable tax withholdings, to be made to holders equal to the excess, if any, of (A) the acquisition price times the number of shares of Stock subject to an Option and Stock Appreciation Right (in each case, to the extent the exercise price does not exceed the acquisition price) over (B) the aggregate exercise price for all such shares of Stock subject to the Option or Stock Appreciation Right as applicable, in exchange for the termination of such Option and Stock Appreciation Right; provided, that if the acquisition price does not exceed the exercise price of any such Option or Stock Appreciation Right, the Committee may cancel that Option and Stock Appreciation Right without the payment of any consideration therefore prior to or upon the Transaction. For purposes of this paragraph 6 and paragraph 7 below, "acquisition price" means the amount of cash, and market value of any other consideration, received in payment for a share of Stock surrendered in a Transaction but need not take into account any deferred consideration unless and until received.

(7) Provide for cash payments, net of applicable tax withholdings, to be made to holder or holders of all or any Awards (other than Options and Stock Appreciation Rights) equal to the acquisition price times the number of shares of Stock subject to any such Awards, in exchange for the termination of any such Awards; provided, that the Committee may cancel, pursuant to paragraph 3 above, any such Award that is subject to a Risk of Forfeiture at the time of the consummation of such Transaction without the payment of any consideration therefor prior to or upon the Transaction.

(8) Provide that, in connection with a liquidation or dissolution of the Company, all or any Awards (other than Restricted Stock or Stock Grants) shall convert into the right to receive liquidation proceeds net of the exercise price thereof and any applicable tax withholdings.

(9) Any combination of the foregoing.

In the event that the Committee determines in its discretion to take the actions contemplated under paragraph (1) above of this Section 8.4(b) with respect to all or any Awards, the Committee shall ensure that, upon consummation of the Transaction, any such Awards are assumed and/or exchanged or replaced with another similar award issued by the acquiring or succeeding entity (or an affiliate thereof) and that, as a result of such assumption and/or exchange or replacement, the holder of such assumed Award and/or such exchanged or replaced similar award has the right to purchase or receive the value of, for each share of Stock subject to such Award immediately prior to the consummation of the Transaction, the consideration (whether cash, securities or other property) received as a result of the Transaction by holders of Stock for each share of Stock held immediately prior to the consummation of the Transaction (and if holders were offered a choice of consideration, the type of consideration chosen by the holders of a majority of the outstanding shares of Stock); *provided, however*, that if such consideration received as a result of the Transaction is not solely common stock (or its equivalent) of the acquiring or succeeding entity (or an affiliate thereof), the Committee may, with the consent of the acquiring or succeeding entity (or an affiliate thereof), provide for the consideration to be received with respect to such assumed Award and/or such exchanged or replaced similar award to consist of or be based solely on common stock (or its equivalent) of the acquiring or succeeding entity (or an affiliate thereof) equivalent in value to the per share consideration received by holders of outstanding shares of Stock as a result of the Transaction; and *provided, further*, that if such Award is an Option, the holder of such Option must exercise the Option and make payment of the applicable exercise price in connection therewith in order to receive such consideration.

(c) Treatment of Other Awards. Upon the occurrence of a Transaction other than a liquidation or dissolution of the Company which is not part of another form of Transaction, then, subject to the provisions of Section 9 below, with respect to all outstanding Awards (other than Options and Stock Appreciation Rights) that are not terminated prior to or upon such Transaction, the repurchase and other rights of the Company under each such Award shall inure to the benefit of the Company's successor and any forfeiture restrictions shall continue to apply and shall, unless the Committee determines otherwise, apply to the cash, securities or other property which the Stock was converted into or exchanged for pursuant to such Transaction in the same manner and to the same extent as they applied to the Award.

(d) Related Matters. In taking any of the actions permitted under this Section 8.4, the Committee shall not be obligated to treat all Awards, all Awards held by a Participant, or all Awards of the same type, identically. Any determinations required to carry out the foregoing provisions of this Section 8.4, including but not limited to the market value of other consideration received by holders of Stock in a Transaction and whether substantially equivalent Rights have been substituted, shall be made by the Committee acting in its sole discretion. In connection with any action or actions taken by the Committee in respect of Awards and in connection with a Transaction, the Committee may require such acknowledgements of satisfaction and releases from Participants as it may determine.

**9. Change of Control**

Except as otherwise provided below, upon the occurrence of a Change of Control, to the extent that the surviving entity declines to continue, convert, assume or replace outstanding Awards, then, notwithstanding anything express or implied to the contrary in Section 8.4 above:

(a) any and all Options and Stock Appreciation Rights not already exercisable in full shall Accelerate with respect to 100% of the shares for which such Options or Stock Appreciation Rights are not then exercisable;

(b) any Risk of Forfeiture applicable to Restricted Stock and Restricted Stock Units which is not based on achievement of Performance Goals or other business objectives shall lapse with respect to 100% of the Restricted Stock and Restricted Stock Units still subject to such Risk of Forfeiture immediately prior to the Change of Control; and

(c) all outstanding Awards of Restricted Stock and Restricted Stock Units conditioned on the achievement of Performance Goals or other business objectives and the payouts attainable under outstanding Performance Units shall be deemed to have been satisfied at target as of the effective date of the Change of Control, except if and to the extent otherwise determined by the Committee in its sole discretion at any time prior to, or upon, such Change of Control.

All such Awards of Performance Units and Restricted Stock Units shall be paid to the extent earned to Participants in accordance with their terms within thirty (30) days following the effective date of the Change of Control. None of the foregoing shall apply, however, (i) in the case of any Award pursuant to an Award Agreement requiring other or additional terms upon a Change of Control (or similar event), (ii) if specifically prohibited under applicable laws, or by the rules and regulations of any governing governmental agencies or national securities exchanges, or (iii) as otherwise provided in Section 7.7, concerning Qualified Performance-Based Awards.

**10. Settlement of Awards**

10.1. In General. Options and Restricted Stock shall be settled in accordance with their terms. All other Awards may be settled in cash, Stock, or other Awards, or a combination thereof, as determined

by the Committee at or after grant and subject to any contrary Award Agreement. The Committee may not require settlement of any Award in Stock pursuant to the immediately preceding sentence to the extent issuance of such Stock would be prohibited or unreasonably delayed by reason of any other provision of the Plan.

10.2. Violation of Law. Notwithstanding any other provision of the Plan or the relevant Award Agreement, if, at any time, in the reasonable opinion of the Company, the issuance of shares of Stock covered by an Award may constitute a violation of law, then the Company may delay such issuance until (i) approval shall have been obtained from such governmental agencies, other than the Securities and Exchange Commission, as may be required under any applicable law, rule, or regulation and (ii) in the case where such issuance would constitute a violation of a law administered by or a regulation of the Securities and Exchange Commission, one of the following conditions shall have been satisfied:

(a) the shares of Stock are at the time of the issue of such shares effectively registered under the Securities Act of 1933, as amended; or

(b) the Company shall have determined, on such basis as it deems appropriate (including an opinion of counsel in form and substance satisfactory to the Company) that the sale, transfer, assignment, pledge, encumbrance or other disposition of such shares does not require registration under the Securities Act of 1933, as amended or any applicable State securities laws.

Furthermore, the inability of the Company to obtain or maintain, or the impracticability of it obtaining or maintaining, authority from any governmental agency having jurisdiction, which authority is deemed by the Company's counsel to be necessary to the lawful issuance of any Stock hereunder, shall relieve the Company of any liability in respect of the failure to issue such Stock as to which such requisite authority shall not have been obtained, and shall constitute circumstances in which the Committee may determine to amend or cancel Awards pertaining to such Stock, with or without consideration to the affected Participants.

10.3. Corporate Restrictions on Rights in Stock. Any Stock to be issued pursuant to Awards granted under the Plan shall be subject to all restrictions upon the transfer thereof which may be now or hereafter imposed by the certificate of incorporation, and bylaws.

10.4. Investment Representations. The Company shall be under no obligation to issue any shares of Stock covered by any Award unless the shares to be issued pursuant to Awards granted under the Plan have been effectively registered under the Securities Act of 1933, as amended, or the Participant shall have made such written representations to the Company (upon which the Company believes it may reasonably rely) as the Company may deem necessary or appropriate for purposes of confirming that the issuance of such shares will be exempt from the registration requirements of that Act and any applicable state securities laws and otherwise in compliance with all applicable laws, rules and regulations of any jurisdiction in which Participants may reside or primarily work, including but not limited to that the Participant is acquiring the shares for his or her own account for the purpose of investment and not with a view to, or for sale in connection with, the distribution of any such shares.

10.5. Registration. If the Company shall deem it necessary or desirable to register under the Securities Act of 1933, as amended, or other applicable statutes any shares of Stock issued or to be issued pursuant to Awards granted under the Plan, or to qualify any such shares of Stock for exemption from the Securities Act of 1933, as amended or other applicable statutes, then the Company shall take such action at its own expense. The Company may require from each recipient of an Award, or each holder of shares of Stock acquired pursuant to the Plan, such information in writing for use in any registration statement, prospectus, preliminary prospectus or offering circular as is reasonably necessary for that purpose and may require reasonable indemnity to the Company and its officers and directors from that holder against all

losses, claims, damage and liabilities arising from use of the information so furnished and caused by any untrue statement of any material fact therein or caused by the omission to state a material fact required to be stated therein or necessary to make the statements therein not misleading in the light of the circumstances under which they were made. In addition, the Company may require of any such person that he or she agree that, without the prior written consent of the Company or the managing underwriter in any public offering of shares of Stock, he or she will not sell, make any short sale of, loan, grant any option for the purchase of, pledge or otherwise encumber, or otherwise dispose of, any shares of Stock during the 180 day period commencing on the effective date of the registration statement relating to the underwritten public offering of securities (or during such shorter or longer period of time as the Committee shall determine in its sole discretion, which period of time shall commence from and after such effective date of such registration statement). Without limiting the generality of the foregoing provisions of this Section 10.5, if in connection with any underwritten public offering of securities of the Company the managing underwriter of such offering requires that the Company's directors and officers enter into a lock-up agreement containing provisions that are more restrictive than the provisions set forth in the preceding sentence, then (a) each holder of shares of Stock acquired pursuant to the Plan (regardless of whether such person has complied or complies with the provisions of clause (b) below) shall be bound by, and shall be deemed to have agreed to, the same lock-up terms as those to which the Company's directors and officers are required to adhere; and (b) at the request of the Company or such managing underwriter, each such person shall execute and deliver a lock-up agreement in form and substance equivalent to that which is required to be executed by the Company's directors and officers.

10.6. Placement of Legends; Stop Orders; etc. Each share of Stock to be issued pursuant to Awards granted under the Plan may bear a reference to the investment representations made in accordance with Section 10.4 in addition to any other applicable restrictions under the Plan, and the terms of the Award and, if applicable, to the fact that no registration statement has been filed with the Securities and Exchange Commission in respect to such shares of Stock. All shares of Stock or other securities issued under the Plan shall be subject to such stop transfer orders and other restrictions as the Committee may deem advisable under the rules, regulations, and other requirements of any stock exchange upon which the Stock is then listed, and any applicable federal or state securities law, and the Committee may cause a legend or legends to be placed on any such certificates to make appropriate reference to such restrictions, or, if the Stock will be held in book-entry position through the direct registration system of the Company's transfer agent, the restrictions will be appropriately noted.

10.7. Tax Withholding. Whenever shares of Stock are issued or to be issued pursuant to Awards granted under the Plan, the Company shall have the right to require the recipient to remit to the Company an amount sufficient to satisfy federal, state, local, foreign or other withholding tax requirements if, when, and to the extent required by law (whether so required to secure for the Company an otherwise available tax deduction or otherwise) prior to the delivery of any certificate or certificates, held in book-entry position through the direct registration system of the Company's transfer agent, for such shares. The obligations of the Company under the Plan shall be conditional on satisfaction of all such withholding obligations and the Company shall, to the extent permitted by law, have the right to deduct any such taxes from any payment of any kind otherwise due to a Participant or to utilize any other withholding method prescribed by the Committee from time to time. However, in such cases Participants may elect, subject to the approval of the Committee, acting in its sole discretion, to satisfy an applicable withholding requirement, in whole or in part, by having the Company withhold shares of Stock to satisfy their tax obligations. All elections shall be irrevocable, made in writing, signed by the Participant, and shall be subject to any restrictions or limitations that the Committee deems appropriate. If shares of Stock are withheld to satisfy an applicable withholding requirement, the shares of Stock withheld shall have a Market Value on the date the tax is to be determined equal to the minimum statutory total tax (or tax calculated at such higher rates as determined by the Committee) which could be imposed on the transaction.

10.8. Company Certificate of Incorporation and Bylaws; Other Company Policies. This Plan and all Awards granted hereunder are subject to the certificate of incorporation and bylaws of the Company, as they may be amended from time to time, and all other Company policies duly adopted by the Board, the Committee or any other committee of the Board and as in effect from time to time regarding the acquisition, ownership or sale of Stock by officers, employees, directors, consultants, advisors and other service providers, including, without limitation, policies intended to limit the potential for insider trading and to avoid or recover compensation payable or paid on the basis of inaccurate financial results or statements, employee conduct, and other similar events.

**11. Reservation of Stock**

The Company shall at all times during the term of the Plan and any outstanding Awards granted hereunder reserve or otherwise keep available such number of shares of Stock as will be sufficient to satisfy the requirements of the Plan (if then in effect) and the Awards and shall pay all fees and expenses necessarily incurred by the Company in connection therewith.

**12. Limitation of Rights in Stock; No Special Service Rights**

A Participant shall not be deemed for any purpose to be a stockholder of the Company with respect to any of the shares of Stock subject to an Award, unless and until a certificate shall have been issued therefor and delivered to the Participant or his agent, or the Stock shall be issued through the direct registration system of the Company's transfer agent. Any Stock to be issued pursuant to Awards granted under the Plan shall be subject to all restrictions upon the transfer thereof which may be now or hereafter imposed by the certificate of incorporation and the bylaws of the Company. Nothing contained in the Plan or in any Award Agreement shall confer upon any recipient of an Award any right with respect to the continuation of his or her employment or other association with the Company (or any Affiliate), or interfere in any way with the right of the Company (or any Affiliate), subject to the terms of any separate employment or consulting agreement or provision of law or certificate of incorporation or bylaws to the contrary, at any time to terminate such employment or consulting agreement or to increase or decrease, or otherwise adjust, the other terms and conditions of the recipient's employment or other association with the Company and its Affiliates.

**13. Unfunded Status of Plan**

The Plan is intended to constitute an "unfunded" plan for incentive compensation, and the Plan is not intended to constitute a plan subject to the provisions of the Employee Retirement Income Security Act of 1974, as amended. With respect to any payments not yet made to a Participant by the Company, nothing contained herein shall give any such Participant any rights that are greater than those of a general creditor of the Company. In its sole discretion, the Committee may authorize the creation of trusts or other arrangements to meet the obligations created under the Plan to deliver Stock or payments with respect to Awards hereunder, provided, however, that the existence of such trusts or other arrangements is consistent with the unfunded status of the Plan.

**14. Nonexclusivity of the Plan**

Neither the adoption of the Plan by the Board nor any action taken in connection with the adoption or operation of the Plan shall be construed as creating any limitations on the power of the Board to adopt such other incentive arrangements as it may deem desirable, including without limitation, the granting of stock options and restricted stock other than under the Plan, and such arrangements may be either applicable generally or only in specific cases.

**15. No Guarantee of Tax Consequences**

It is intended that all Awards shall be granted and maintained on a basis which ensures they are exempt from, or otherwise compliant with, the requirements of Section 409A of the Code, pertaining non-qualified plans of deferred compensation, and the Plan shall be governed, interpreted and enforced consistent with such intent. However, neither the Company nor any Affiliate, nor any director, officer, agent, representative or employee of either, guarantees to the Participant or any other person any particular tax consequences as a result of the grant of, exercise of rights under, or payment in respect of an Award, including but not limited to that an Option granted as an Incentive Option has or will qualify as an "incentive stock option" within the meaning of Section 422 of the Code or that the provisions and penalties of Section 409A of the Code will or will not apply and no person shall have any liability to a Participant or any other party if a payment under an Award that is intended to benefit from favorable tax treatment or avoid adverse tax treatment fails to realize such intention or for any action taken by the Board or the Committee with respect to the Award.

**16. Termination and Amendment of the Plan**

16.1. Termination or Amendment of the Plan. Subject to the limitations contained in Section 16.3 below, including specifically the requirement of stockholder approval, if applicable, the Committee may at any time suspend or terminate the Plan or make such modifications of the Plan as it shall deem advisable. Unless the Committee otherwise expressly provides, no amendment of the Plan shall affect the terms of any Award outstanding on the date of such amendment.

16.2. Termination or Amendment of Outstanding Awards; Assumptions. Subject to the limitations contained in Section 16.3 below, including specifically the requirement of stockholder approval, if applicable, the Committee may at any time:

(a) amend the terms of any Award theretofore granted, prospectively or retroactively, provided that the Award as amended is consistent with the terms of the Plan;

(b) within the limitations of the Plan, modify, extend or assume outstanding Awards or accept the cancellation of outstanding Awards or of outstanding stock options or other equity-based compensation awards granted by another issuer in return for the grant of new Awards for the same or a different number of shares of Stock and on the same or different terms and conditions (including but not limited to the exercise price of any Option); and

(c) offer to buy out for a payment in cash or cash equivalents an Award previously granted or authorize the recipient of an Award to elect to cash out an Award previously granted, in either case at such time and based upon such terms and conditions as the Committee shall establish.

16.3. Limitations on Amendments, Etc.

(a) Without the approval of the Company's stockholders, no amendment or modification of the Plan by the Committee may (i) increase the number of shares of Stock which may be issued under the Plan, (ii) change the description of the persons eligible for Awards, or (iii) effect any other change for which stockholder approval is required by law or the rules of any relevant stock exchange. Awards may be made under the Plan that involve shares of Stock in excess of the number of shares then available for issuance under the Plan, provided no shares shall actually be issued pursuant to those Awards until the number of shares of Stock available for issuance under the Plan is sufficiently increased by stockholder approval of an amendment of the Plan authorizing such increase. If such stockholder approval

is not obtained within twelve (12) months after the date the first excess Award is made, then all Awards granted on the basis of such excess shares shall terminate and cease to be outstanding.

(b) No action by the Board or the Committee pursuant to this Section 16 shall impair the rights of the recipient of any Award outstanding on the date of such amendment or modification of such Award, as the case may be, without the Participant's consent; *provided, however,* that no such consent shall be required (A) in the case of any amendment or termination of any outstanding Award that is permitted by any provision of this Plan that is set forth in Section 8, Section 9 or in any other section of this Plan that is not Section 16.2 or (B) if the Board or Committee, as the case may be, (i) determines in its sole discretion and prior to the date of any Change of Control that such amendment or alteration either is required or advisable in order for the Company, the Plan or the Award to satisfy any law or regulation, including without limitation the provisions of Section 409A of the Code, or to meet the requirements of or avoid adverse financial accounting consequences under any accounting standard, (ii) determines in its sole discretion and prior to the date of any Change of Control that such amendment or alteration is not reasonably likely to significantly diminish the benefits provided under the Award, or that any such diminution has been adequately compensated, or (iii) reasonably determines on or after the date of Change of Control that such amendment or alteration either is required or advisable in order for the Company, the Plan or the Award to satisfy any law or regulation, including without limitation the provisions of Section 409A of the Code.

**17. Recoupment**

Participants shall be subject to any clawback, recoupment or other similar policy adopted by the Board as in effect from time to time and Awards and any cash, shares of Stock or other property or amounts due, paid or issued to a Participant shall be subject to the terms of such policy, as in effect from time to time.

**18. Notices and Other Communications**

Any communication or notice required or permitted to be given under the Plan shall be in such form as the Committee may determine from time to time. If a notice, demand, request or other communication is required or permitted to be given in writing, then any such notice, demand, request or other communication hereunder to any party shall be deemed to be sufficient if contained in a written instrument delivered in person or duly sent by first class registered, certified or overnight mail, postage prepaid, or by facsimile with a confirmation copy by regular, certified or overnight mail, addressed or by facsimile, as the case may be, (i) if to the recipient of an Award, at his or her residence address last filed with the Company and (ii) if to the Company, at its principal place of business, addressed to the attention of its Treasurer, or to such other address or facsimile number, as the case may be, as the addressee may have designated by notice to the addressor. All such notices, requests, demands and other communications shall be deemed to have been received: (i) in the case of personal delivery, on the date of such delivery; (ii) in the case of mailing, when received by the addressee; and (iii) in the case of facsimile transmission, when confirmed by facsimile machine report.

**19. Governing Law**

The Plan and all Award Agreements and actions taken hereunder and thereunder shall be governed, interpreted and enforced in accordance with the laws of the State of Delaware, without regard to the conflict of laws principles thereof.

*[End of document.]*

**RHYTHM PHARMACEUTICALS, INC.**
**2017 EQUITY INCENTIVE PLAN**

**Stock Option Agreement**

**This Stock Option Agreement,** dated as of [_____, 20__] (this "Agreement"), is between Rhythm Pharmaceuticals, Inc., a corporation organized under the laws of the State of Delaware (the "Company"), and the individual identified in paragraph 1 below, currently residing at the address set out at the end of this Agreement (the "Optionee"). Capitalized terms used in this Agreement without definition shall have the respective meaning ascribed to such capitalized terms in the Plan (as defined below).

**1. Grant of Option.** Pursuant and subject to the Company's 2017 Equity Incentive Plan (as the same may be amended from time to time, the "Plan"), the Company grants to you, the Optionee identified in the table below, an option (the "Option") to purchase from the Company all or any part of a total of the number of shares identified in the table below (the "Optioned Shares") of the common stock, par value $0.001 per share, in the Company (the "Stock"), at the exercise price per share set out in the table below.

**Optionee** _____

**Number of Shares** _____

**Exercise Price Per Share** _____

**Grant Date** _____

**Expiration Date**[1] _____

**2. Character of Option.** This Option [is/is not][2] intended to be treated as an "incentive stock option" within the meaning of Section 422 of the Internal Revenue Code of 1986, as amended.

**3. Expiration of Option.** This Option shall expire at 5:00 p.m. EST on the Expiration Date or, if earlier, the earliest of the dates specified in whichever of the following applies:

a) If the termination of your employment or other association is on account of your death or disability, the first anniversary of the date your employment ends.

b) If the termination of your employment or other association is due to any other reason, three (3) months after your employment or other association ends.

[1] For ISOs, not later than the day immediately preceding the tenth anniversary of the Grant Date.

[2] Either "is" or "is not", as the Committee or the Board has determined.

**4. Exercise of Option.**

a) You may exercise this Option, in full or in part and at any time prior to the date this Option expires, as to the number of Optioned Shares for which this Option shall have become exercisable (the "Vested Shares") pursuant Section 4(b) below. However, during any period that this Option remains outstanding after the end of your association with the Company and its Affiliates in any and all capacities as an officer, director, employee and/or consultant of the Company and its Affiliates, you may exercise it only to the extent of any remaining Vested Shares determined as of the effective time of the end of such association. The procedure for exercising this Option is described in Section 7.1(f) of the Plan; provided that in no event shall a fraction of a share of Stock be purchasable or deliverable upon exercise.

b) [Vesting terms to be inserted]

c)

| Number of Shares in Each Installment | Initial Exercise Date for Shares in Installment |
|---|---|

**5. Transfer of Option.** You may not transfer this Option except by will or the laws of descent and distribution, and, during your lifetime, only you may exercise this Option.

**6. Incorporation of Plan Terms.** This Option is granted subject to all of the applicable terms and provisions of the Plan, including but not limited to the limitations on the Company's obligation to deliver Optioned Shares upon exercise set forth in Section 9 therein.

**7. Tax Consequences.** The Company makes no representation or warranty as to the tax treatment to you of your receipt or exercise of this Option or upon your sale or other disposition of the Optioned Shares. You should rely on your own tax advisors for such advice.

**8. Treatment as Wages or Compensation.** No amounts paid or payable in connection with this Option shall constitute wages or compensation for purposes of any applicable law, if ever, prior to the date on which such amount has been earned, vested and become payable in accordance with the terms of this Agreement and the Plan. No such amount shall be treated as wages or compensation for purposes of any employee or other benefit plan of the Company and its Affiliates except to the extent and at the time provided in the respective employee or other benefit plan.

**9. Acknowledgements.** You acknowledge that you have reviewed and understand the Plan and this Agreement in their entirety, and have had an opportunity to obtain the advice of counsel prior to executing this Agreement. You hereby agree to accept as binding, conclusive and final all decisions or interpretations of the Committee upon any questions arising under the Plan or this Agreement.

**10. Further Assurances.** The parties agree to execute such further instruments and to take such action as may reasonably be necessary to carry out the intent of this Agreement.

[**11. Community Property.** Without prejudice to the actual rights of the spouses as between each other, for all purposes of this Agreement, you shall be treated as agent and attorney-in-fact for that interest held or claimed by your spouse with respect to this Option and any Optioned Shares and the parties hereto shall act in all matters as if the Optionee was the sole owner of this Option and (following exercise) any such Optioned Shares. This appointment is coupled with an interest and is irrevocable.][3]

**12. Miscellaneous.** This Agreement shall be construed and enforced in accordance with the laws of the State of Delaware, without regard to the conflict of laws principles thereof and shall be binding upon and inure to the benefit of any successor or assign of the Company and any executor, administrator, trustee, guardian, or other legal representative of you. Capitalized terms used but not defined herein shall have the meaning assigned under the Plan. This Agreement may be executed in one or more counterparts all of which together shall constitute but one instrument. In making proof of this Agreement it shall not be necessary to produce or account for more than one such counterpart.

*[The remainder of this page is intentionally left blank. Signature page to follow.]*

[3] Consider for inclusion for grants to California residents (and residents of other states with community property rules).

**RHYTHM PHARMACEUTICALS, INC.**
**2017 EQUITY INCENTIVE PLAN**

**Option Exercise Form**

Rhythm Pharmaceuticals, Inc.
500 Boylston Street, 11th Floor
Boston, MA 02116

Attention: Controller

Dear Sir:

In accordance with, and subject to the terms and conditions of, the Rhythm Pharmaceuticals, Inc. 2017 Equity Incentive Plan, as amended and in effect to date, I hereby elect to exercise my option granted under the agreement dated _____, to purchase _____ shares of the common stock, par value $0.001 per share, in Rhythm Pharmaceuticals, Inc. (the "Company").

Enclosed herewith is payment to the Company in the amount of $_____ in full payment of the option price of $_____ per share, for said shares. [*To be revised as necessary for non-cash payment of exercise price*.]

Sincerely yours,

_____
Name:

**Exhibit 31.1**

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 14, 2017

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

**Exhibit 31.2**

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 14, 2017

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

**Exhibit 32.1**

**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, 2017 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 14, 2017

**Exhibit 32.2**

**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, 2017 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 14, 2017