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Mast Therapeutics, Inc.
Form 10-K
March 06, 2017

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2016

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 No. 001-32157

Mast Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of

incorporation or organization)

3611 Valley Centre Dr., Suite 500, San Diego, CA
(Address of principal executive offices)

84-1318182
(I.R.S. Employer

Identification No.)

92130
(Zip Code)

(858) 552-0866

(Registrant's telephone number, including area code)

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Securities registered pursuant to Section 12(b) of the Act:

Title of each class:	Name of each exchange on which registered:
Common Stock, par value \$0.001 per share	NYSE MKT LLC

Securities registered pursuant to Section 12(g) of the Act:

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes No

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 periods 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 Website, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) 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 if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statement incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

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

Large accelerated filer Accelerated filer

Non-accelerated filer Smaller reporting company

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant as of June 30, 2016 was approximately \$96.1 million based upon the closing price of the registrant's common stock on the NYSE MKT reported for such date.

As of March 2, 2017, the registrant had 254,746,933 shares of its common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Not applicable.

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Cautionary Statement Concerning Forward-Looking Statements

This Annual Report on Form 10-K, particularly in Item 1 “Business,” and Item 7 “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” and the information incorporated herein by reference, include forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These forward-looking statements are based on current expectations and beliefs and involve numerous risks and uncertainties that could cause actual results to differ materially from expectations. These forward-looking statements should not be relied upon as predictions of future events as we cannot assure you that the events or circumstances reflected in these statements will be achieved or will occur. When used in this report, the words “believe,” “may,” “could,” “will,” “estimate,” “continue,” “anticipate,” “intend,” “expect,” “indicate,” “seek,” “should,” “would” and similar expressions are intended to identify forward-looking statements, though not all forward-looking statements contain these identifying words. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements. For example, forward-looking statements include, but are not limited to statements about:

- plans intended to alleviate the substantial doubt about our ability to continue as a going concern, including the proposed merger with Savara and related transactions;
- plans, strategies and objectives for future operations, including the execution and timing of those plans, including with regard to the proposed merger with Savara and related transactions;
- the likelihood of the satisfaction or waiver of conditions to the completion of the proposed merger with Savara and whether and when the merger will be consummated;
- our future financial condition or performance;
- prospects for regulatory approval of our product candidates, including timing and outcomes of clinical studies;
- prospects for market success of our product candidates, including competition, intellectual property protection and infringement, third party payor coverage and reimbursement; and
- our continued listing on the NYSE MKT or listing on any other national securities exchange;

For a discussion of the factors that may cause our actual results, performance or achievements to differ materially from any future results, performance or achievements expressed or implied in such forward-looking statements, or for a discussion of risk associated with completing the proposed merger with Savara and the combined organization, see Part I, Item 1A, “Risk Factors,” in this report.

If any of these risks or uncertainties materializes or any of these assumptions proves incorrect, our results could differ materially from the forward-looking statements in this report. All forward-looking statements in this report are current only as of the date of this report. We do not undertake any obligation to publicly update any forward-looking statement to reflect events or circumstances after the date on which any statement is made or to reflect the occurrence of unanticipated events.

Unless context requires otherwise, all references in this report to “Mast,” our company,” “we,” “us,” “our,” or similar words refer to Mast Therapeutics, Inc. together with its consolidated subsidiaries.

PART I

Item 1. Business.

Overview

We are a biopharmaceutical company developing novel, clinical-stage therapies for serious or life-threatening diseases with significant unmet needs. Our lead product candidate, AIR001, a sodium nitrite solution for inhalation via nebulization, is in Phase 2 clinical development for the treatment of heart failure with preserved ejection fraction, or HFpEF, also known as diastolic heart failure or heart failure with preserved systolic function. Data show there are approximately 5.7 million individuals with heart failure in the U.S. and that approximately 50% of patients hospitalized for heart failure have HFpEF. Enrollment is ongoing in three investigator-sponsored Phase 2 studies of AIR001 in patients with HFpEF being conducted at prestigious research institutions. Positive interim results from one of those studies were published in November 2016. Additionally, positive results from a completed Phase 2 study of AIR001 in patients with HFpEF were published in July 2016. We anticipate results from one of the ongoing studies, a multicenter, randomized, double-blind, placebo-controlled crossover Phase 2 study of AIR001 in HFpEF being conducted by the Heart Failure Clinical Research Network (known as the HFN) in the first quarter of 2018.

Previously, our vepoloxamer product candidate was in Phase 3 clinical development for treatment of vaso-occlusive crisis in patients with sickle cell disease and Phase 2 clinical development for treatment of heart failure with reduced ejection fraction, but, in September 2016, after the Phase 3 study failed to achieve its primary efficacy endpoint, we made the strategic decision to discontinue clinical development of vepoloxamer and wind down all of the clinical studies of that asset. We have since limited our development of vepoloxamer to an NIH grant-funded nonclinical study in ischemic stroke in order to focus our resources on AIR001's development.

During the fourth quarter of 2016, we restructured our organization to better align our workforce with our revised operating plans, which include supporting three ongoing investigator-sponsored Phase 2 studies of AIR001 in patients with HFpEF and one Phase 1/2 study in patients with cystic fibrosis, as discussed in more detail below. We have reduced our full-time workforce by more than 70% since the beginning of the fourth quarter of 2016 to a total of six remaining positions.

Proposed Merger with Savara and Change in Control

In January 2017, after an extensive review of strategic alternatives and a thorough process during which our board of directors, with assistance from its strategic transactions committee consisting of independent directors, considered a multitude of factors, our board of directors unanimously approved and we entered into the Agreement and Plan of Merger and Reorganization, dated January 6, 2017, with Savara Inc., a privately-held, clinical-stage specialty pharmaceutical company focused on the development and commercialization of novel therapies for the treatment of serious or life-threatening rare respiratory diseases. Pursuant to the merger agreement, subject to the satisfaction or waiver of the conditions set forth in the agreement, Victoria Merger Corp., our wholly-owned subsidiary formed solely for purposes of carrying out the merger, will merge with and into Savara, with Savara surviving the merger as a wholly-owned subsidiary of our company and Savara stockholders receiving newly issued shares of our common stock in exchange for their Savara stock. The Merger is intended to qualify for federal income tax purposes as a tax-free reorganization under the provisions of Section 368(a) of the Internal Revenue Code of 1986, as amended. The transactions contemplated by the merger agreement will result in a change in control of our company as described below. The transaction is expected to close in the second quarter of 2017.

The merger agreement contemplates that, immediately following the merger, the combined company's name will be changed from "Mast Therapeutics, Inc." to "Savara Inc.," the board of directors will consist of seven members, five of which will be the current directors of Savara and two of which will be independent directors designated by us, which

are expected to be two of our current independent directors, and the executive officers of the combined company will be designated by Savara with Savara's Chief Executive Officer, Robert Neville, being the combined company's Chief Executive Officer, and Savara's Chief Financial Officer, David Lowrance, being the combined company's Chief Financial Officer. The combined company's pipeline would include:

- AeroVanc, an inhaled dry-powder vancomycin to treat chronic methicillin-resistant *Staphylococcus aureus* (MRSA) pulmonary infection in cystic fibrosis, which is in preparation for a pivotal Phase 3 clinical study;
- Molgradex, an inhaled nebulized GM-CSF to treat pulmonary alveolar proteinosis (PAP), which is currently in Phase 2/3 development; and
- AIR001, our lead product candidate.

Subject to the terms and conditions of the merger agreement, at the effective time of the merger, (a) each outstanding share of Savara common stock, on an as-converted basis taking into consideration all outstanding common stock, preferred stock, restricted

stock and all other securities convertible or exercisable for Savara common stock, will be converted into the right to receive the number of shares of our common stock equal to the exchange ratio described below; (b) each outstanding Savara stock option that has not previously been exercised will be assumed by us; and (c) each outstanding warrant to acquire Savara capital stock that has not previously been exercised will be assumed by us.

Under the exchange ratio formula in the merger agreement, as of immediately after the merger, but excluding the effect of certain financings (as further described in the merger agreement), the former Savara securityholders are expected to own approximately 76% of the aggregate number of shares of our common stock issued and outstanding following the consummation of the merger (referred to as the Post-Closing Shares), and the stockholders of Mast as of immediately prior to the merger are expected to own approximately 24% of the aggregate number of Post-Closing Shares. These percentage ownership figures are estimates. The exchange ratio will be fixed prior to closing to reflect Mast's and Savara's capitalization as of immediately prior to the merger. In addition, to the extent our net cash at closing (as "net cash" is specifically defined in the merger agreement), is less than zero dollars, the exchange ratio may be further adjusted in a manner that would reduce the percentage of the aggregate number of Post-Closing Shares held by stockholders of Mast as of immediately prior to the merger.

The merger agreement contains customary representations, warranties and covenants made by Mast and Savara, including covenants relating to obtaining the requisite approvals of the stockholders of Mast and Savara, indemnification of directors and officers, and Mast's and Savara's conduct of our respective businesses between the date of signing the merger agreement and the closing of the merger. Consummation of the merger is subject to certain closing conditions, including, among other things, approval by the stockholders of Mast and Savara. The merger agreement contains certain termination rights for both Mast and Savara, and further provides that, upon termination of the merger agreement under specified circumstances, we may be required to pay Savara a termination fee of \$1.8 million or Savara may be required to pay us a termination fee of \$2.5 million.

In addition to seeking stockholder approval of the merger agreement and issuance of shares to the Savara securityholders, we will also seek stockholder approval to effect a reverse stock split intended to increase the market price of our common stock above the minimum requirements of the NYSE MKT, LLC for initial listing and to provide for sufficient authorized and unissued shares for the issuance of shares to the Savara securityholders. Subject to stockholder approval, we would implement the reverse stock split at a ratio to be mutually agreed to by us and Savara.

Concurrently with the execution of the merger agreement, the officers and directors of Mast entered into a voting agreement with Mast, and the officers, directors and certain affiliated stockholders of Savara entered into a voting agreement with Savara. These voting agreements place certain restrictions on the transfer of the shares of Mast and Savara held by the respective signatories thereto and include covenants as to the voting of such shares in favor of approving the transactions contemplated by the merger agreement and against any actions that could adversely affect the consummation of the Merger.

Concurrently with the execution of the merger agreement, the officers and directors of the Mast and the officers, directors and certain stockholders of Savara entered into lock-up agreements pursuant to which they have agreed, among other things, not to sell or dispose of any shares of our common stock which are or will be beneficially owned by them at the closing of the merger with one third (1/3) of such shares being released from such restrictions on each of (i) the six (6) month anniversary, (ii) the eight (8) month anniversary and (iii) the ten (10) month anniversary of the effective time of the merger.

The descriptions above of merger agreement, the voting agreements, and the lock-up agreements do not purport to be complete and are qualified in their entirety by reference to the merger agreement, the forms of the voting agreements, and the forms of lock-up agreement and the amendment to the lock-up agreement that have filed with the Securities

and Exchange Commission, or the SEC, and are incorporated by reference in this report. The assertions embodied in the representations and warranties contained in the merger agreement are qualified by information in confidential disclosure schedules delivered by the parties in connection with the signing of the merger agreement. Moreover, certain representations and warranties contained in these agreements were made as of a specified date; may have been made for the purposes of allocating contractual risk between the parties to such agreements; and may be subject to contractual standards of materiality different from what might be viewed as material to our stockholders. Accordingly, the representations and warranties in these agreements should not be relied on by any persons as characterizations of the actual state of facts and circumstances of the Company or any other parties thereto at the time they were made and should consider the information in these agreements in conjunction with the entirety of the factual disclosure about our company in this annual report. Information concerning the subject matter of the representations and warranties may have changed after the date of these agreements, which subsequent information may or may not be fully reflected in our public disclosures. These agreements should not be read alone, but should instead be read in conjunction with each other and other information included in this report.

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AIR001

AIR001 is a sodium nitrite solution for intermittent inhalation via nebulization. Nitrite is a direct vasodilator and can be recycled in vivo to form nitric oxide (NO) independent of the classical NO synthase (NOS) pathway. Nitrite-mediated NO formation has several beneficial effects, including dilation of blood vessels and reduction of inflammation and undesirable cell growth. Generation of NO from sodium nitrite is not dependent upon endothelial function and is enhanced in the setting of tissue hypoxia and acidosis, conditions in which NOS activity typically is depressed. In experimental models, nitrite use has demonstrated improved remodeling both in the pulmonary vasculature and right ventricle. Hemodynamic effects include venodilation with reductions in right atrial pressures, pulmonary and systemic vasodilation with reductions in pulmonary vascular resistance and left atrial pressures, and improved cardiac relaxation. In addition, nonclinical studies have demonstrated that nitrite can stimulate mitochondrial biogenesis and mitochondrial fusion and decrease mitochondrial oxygen consumption through a mechanism distinct from that of NO, which may have additional effects to improve exercise tolerance in heart failure.

We obtained the AIR001 program through our acquisition of Aires Pharmaceuticals, Inc. in February 2014. Prior to the acquisition, AIR001 had been tested in more than 120 healthy volunteers and patients with various forms of pulmonary hypertension in three Phase 1 studies and one Phase 2 study and was generally well-tolerated. Data from the 29 patients with pulmonary arterial hypertension who enrolled in the Phase 2 study showed a trend toward improvements in hemodynamic parameters and change in exercise capacity from baseline, and AIR001 was generally well-tolerated, with no drug-related serious adverse events. In particular, levels of methemoglobin, which diminishes oxygen carrying capacity, remained normal (< 1.5%), distinguishing AIR001 from safety concerns associated with sodium nitrite injection, a commercially-available product for the treatment of acute cyanide poisoning that contains a black box warning for life-threatening hypotension and methemoglobin formation.

Rationale for Development of AIR001 in HFpEF

We are developing AIR001 for the treatment of patients with HFpEF. Data show that approximately 50% of patients hospitalized for heart failure have HFpEF and the prevalence of HFpEF is expected to increase as the population ages. To date, no pharmacologic agents have shown convincing evidence of efficacy in HFpEF and few interventions have been observed to improve symptoms or quality of life for HFpEF patients.

Patients with HFpEF suffer from dyspnea and fatigue with activity, limiting exercise tolerance. The pathophysiology of HFpEF is complex and includes left ventricular systolic and diastolic dysfunction, pulmonary vascular disease, endothelial dysfunction, and peripheral oxygen utilization abnormalities. In HFpEF patients, cardiac pressures are often normal at rest but elevated with minimal stress (exercise), creating a major barrier to treatment because interventions that reduce filling pressures during exercise also may reduce resting pressures, increasing vulnerability to hypotension. While HFpEF is a heterogeneous syndrome, which may explain the failure of clinical studies testing therapies that have shown efficacy in treating HFrEF, elevation in left ventricular (LV) filling pressures and pulmonary artery pressures during exercise has been a universal finding in HFpEF patients.

Evidence points to impaired nitric oxide-cyclic guanosine monophosphate (NO-cGMP) bioavailability as playing a central role in the abnormalities that limit exercise capacity in HFpEF patients. NO-cGMP levels can be increased using direct NO donors, such as the organic nitrates. However, organic nitrates have shown several shortcomings, including the development of tolerance, greater vulnerability to hypotension in patients with HFpEF, development of “pseudo-tolerance,” where chronic venodilation leads to renal sodium retention, and increases in oxidative stress resulting in endothelial dysfunction. Inorganic nitrite is an alternative strategy to restoring NO-cGMP levels. Notably, because generation of NO from nitrite is enhanced with tissue hypoxia and acidosis, as occur during exercise, it becomes most active at the time of greatest need for HFpEF patients.

Clinical Development in HFpEF

We have supported, or currently are supporting, four investigator-sponsored Phase 2 clinical studies of AIR001 in patients with HFpEF being conducted at prestigious research institutions.

Completed Phase 2 Study in Patients with HFpEF

In February 2016, we reported positive top-line results from a randomized, double-blind, placebo-controlled Phase 2a study of AIR001 in 30 patients with HFpEF referred to the catheterization laboratory for invasive exercise stress testing. Detailed results from the study were published in *Circulation Research* in July 2016 in an article entitled, “Inhaled Sodium Nitrite Improves Rest and Exercise Hemodynamics in Heart Failure With Preserved Ejection Fraction.” In the study, AIR001 showed statistically significant improvement for the pre-specified primary endpoint: change in pulmonary capillary wedge pressure (PCWP) at 20 Watts exercise after drug treatment relative to PCWP at 20 Watts exercise in the initial assessment prior to drug treatment, compared to placebo-treated patients. AIR001 also significantly lowered right atrial pressure and significantly improved pulmonary artery compliance.

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Study data show that nebulized inhaled AIR001 attenuates the hemodynamic derangements of cardiac failure that occur during exercise in HFpEF patients. AIR001 was generally well-tolerated, with no drug-related serious adverse events.

Phase 2 Study in Patients with PH-HFpEF

Enrollment is ongoing in an open-label Phase 2 study evaluating the effect of AIR001 delivered in a dose escalation manner on the change in cardiovascular hemodynamics in subjects with PH who undergo standard right heart catheterization. (ClinicalTrials.gov Identifier: NCT01431313) The study plans to enroll a total of approximately 50 subjects with pulmonary hypertension (PH). Approximately 20 of the subjects will have a diagnosis of PH associated with HFpEF. Subjects receive a first dose of 45 mg of nebulized inhaled AIR001, with one subsequent escalation dosage to 90 mg approximately 60 minutes after the first dose, based on safety and tolerability. During the study, right heart/pulmonary artery hemodynamics are measured continuously, and cardiac output is measured at 15 minute intervals, as well as noninvasive systemic blood pressure and pulse oximetry monitoring. Changes in hemodynamics and calculated pulmonary systemic vascular resistances, as well as pulmonary artery compliance will be performed utilizing standard formulas. The primary efficacy endpoint of the study is the change in pulmonary vascular resistance (PVR) from time zero and at 15, 30 and 45 minutes of nebulization.

Positive interim results from the study, including data on 10 of the 20 PH-HFpEF patients to be enrolled, were published in the Journal of Clinical Investigation in November 2016. Of the 36 subjects whose data was reviewed, 20 were diagnosed with World Health Organization (WHO) Group 1 pulmonary arterial hypertension (PAH) and on background PAH-specific therapy, 10 were diagnosed with PH-HFpEF (WHO Group 2 PH), and 6 were diagnosed with WHO Group 3 PH. In those 36 subjects, administration of nebulized inhaled AIR001 significantly decreased pulmonary, right atrial, and pulmonary capillary wedge pressures, and was most pronounced in the patients with PH-HFpEF. AIR001 administration also led to a substantial increase in pulmonary artery compliance, which was most pronounced in the patients with PH-HFpEF. AIR001 was generally well-tolerated; no significant safety concerns were identified, satisfying the primary safety outcome of the study. In addition, there were no significant decreases in peripheral oxygen saturation nor increases in methemoglobin levels above the stopping criteria of 5%.

In the 10 patients with PH-HFpEF, AIR001 administration resulted in significant overall decreases in right atrial pressure, pulmonary capillary wedge pressure, right ventricular systolic and diastolic, and pulmonary artery systolic, diastolic and mean pressures. Pulmonary capillary wedge pressure and mean pulmonary artery pressure decreased by 7.5 mm Hg (95%CI: -9.0, -6.0) and 7.9 mm Hg (95%CI: -9.4, -6.3), respectively (baseline median values 18 and 34 mm Hg, respectively). There was no significant change in transpulmonary gradient and a modest but significant increase in PVR. Pulmonary artery compliance increased by 35% (+0.97 mL/mm Hg, 95%CI: +0.25, +1.68; P = 0.008).

Further analysis of the dose effect of AIR001 found that most hemodynamics were affected in a dose dependent manner with the exception of pulmonary artery compliance. There was a significant dose effect on right atrial pressure, mean pulmonary artery pressure, and pulmonary capillary wedge pressure. Cardiac index decreased in a dose-dependent manner. The increase in pulmonary artery compliance was not dose related.

The interim data demonstrate that AIR001 can significantly lower right atrial pressures, pulmonary artery pressures, and pulmonary artery occlusion pressures, as well as improve pulmonary artery compliance and support further study in non-Group 1 PH patients.

Phase 2 INDIE-HFpEF Study

In 2016, AIR001 was selected by the Heart Failure Clinical Research Network (known as the HFN) for evaluation in a multicenter, randomized, double-blind, placebo-controlled crossover Phase 2 study in approximately 100 patients with HFpEF known as the Inorganic Nitrite Delivery to Improve Exercise Capacity in HFpEF study, or the INDIE-HFpEF study. The study began in the third quarter of 2016 and patient enrollment is ongoing. (ClinicalTrials.gov Identifier: NCT02742129) Results are expected in the first quarter of 2018. The study is being conducted with significant support from a grant awarded by the National Heart, Lung, and Blood Institute (NHLBI), part of the National Institutes of Health (NIH). We are providing test materials (AIR001 and placebo), drug delivery devices (nebulizers), regulatory and technical support, and some additional financial support, as described in Item 7, “Management’s Discussion and Analysis of Financial Condition and Results of Operations – Liquidity and Capital Resources,” of this report.

The study is a randomized, double-blind, placebo-controlled crossover study to evaluate the effect of AIR001 on peak exercise capacity as assessed by cardiopulmonary exercise testing (CPET). Approximately 100 patients with a diagnosis of HFpEF will be enrolled across approximately 20 clinical centers in the United States that are part of the HFN. The primary efficacy endpoint is the peak oxygen consumption (VO₂) after four weeks of treatment with nebulized inhaled AIR001 or placebo as assessed by CPET performed at peak drug levels. Secondary objectives include (i) submaximal activity tolerance chronically, (ii) quality of life, (iii)

chronic filling pressures as assessed by echocardiography and natriuretic peptide levels, and/or (iv) ventilator efficiency or submaximal exercise capacity at peak drug levels, and evaluation of the safety and tolerability of AIR001.

The HFN is an NHLBI clinical research network. The primary goal of the HFN is to conduct multiple clinical trials to evaluate treatments and strategies to improve management of acute and chronic heart failure. The HFN provides a unique platform for collaborative research by bringing together many premier centers across North America. HFN is composed of nine Regional Coordinating Centers and their affiliated sites, whose investigators provide scientific leadership in the collaborative development of the HFN's scientific agenda. The HFN is recognized for robust enrollment in heart failure clinical trials and high scientific productivity. The goal of partnering with HFN is to accelerate research and medical innovation, and provide early results that may improve public health.

Phase 2 INABLE-TRAINING Study

Enrollment is ongoing in a Phase 2 clinical study of AIR001 in patients with HFpEF known as the Inorganic Nitrite to Amplify the Benefits and Tolerability of Exercise Training study, or the INABLE-TRAINING study. (ClinicalTrials.gov Identifier: NCT02713126) This is a randomized, blinded, placebo-controlled, two-arm, parallel-group study in approximately 68 patients with HFpEF is evaluating AIR001's potential to improve the clinical responses to and tolerability of exercise training (ET) in individuals with HFpEF. The primary endpoint of the study is the change in exercise capacity as measured by peak oxygen consumption (baseline to 12 weeks).

All study subjects will undergo 12 weeks of ET. Subjects will be randomized to receive nebulized inhaled AIR001 three times daily or nebulized inhaled placebo (sodium chloride) three times daily during the study period and will wear accelerometry devices to track daily physical activity at home. After 12 weeks of ET as part of standard cardiac rehabilitation, study subjects will repeat the assessment of cardiovascular function and exercise capacity as performed at study entry to assess efficacy at a final visit.

The INABLE-TRAINING study has 2 aims. First, to determine whether treatment with inhaled AIR001 in addition to ET for 12 weeks improves exercise capacity and hemodynamic reserve in HFpEF. Expired gas analysis, inert gas (C₂H₂) rebreath, and echocardiography will be performed during rest and exercise to measure oxygen consumption (VO₂), CO, and hemodynamics before and after completion of 12 weeks of ET with inhaled NO₂- vs ET with inhaled placebo. Second, to determine whether treatment with inhaled AIR001 in addition to ET for 12 weeks increases daily activity levels and quality of life (QOL), and reduces symptoms of effort intolerance during ET. Tolerability of ET will be assessed by Borg perceived effort and dyspnea scores. Large and small vessel endothelial function (brachial and digital arteries) and QOL will also be assessed. Secondary endpoints include cardiac output reserve, peak exercise workload, rest and exercise hemodynamics assessed by echocardiography, Borg dyspnea and fatigue scores recorded during ET, endothelial function assessed by tonometry and brachial artery flow mediated dilation, and QOL assessed by the Kansas City Cardiomyopathy Questionnaire

Early Clinical Development

Prior to our acquisition of Aires in 2014, AIR001 had been tested in more than 120 healthy volunteers and patients with various forms of pulmonary hypertension in three Phase 1 studies and one Phase 2 study and was generally well-tolerated. Early studies investigated the maximal tolerated dose and potential drug-drug interactions with sildenafil. Additionally, Aires initiated enrollment in a 90-patient Phase 2 study of AIR001 in patients with PAH, which was prematurely terminated by Aires prior to our acquisition of the company due to Aires' capital constraints. Data from the 29 patients who had enrolled in the study showed a trend toward improvements in hemodynamic parameters and change in exercise capacity from baseline and AIR001 was generally well-tolerated, with no drug-related serious adverse events. In particular, methemoglobin levels remained normal (< 1.5%).

Future Development in HFpEF

The primary efficacy endpoint of the INDIE-HFpEF study, change in aerobic capacity (peak VO₂, as assessed by cardiopulmonary exercise testing (CPET)), has been correlated with other measures of improved exercise function such as six minute walk distance (6MWD) and survival. Secondary measures in that study include whether AIR001 improves submaximal activity as measured by accelerometry and quality of life on the Kansas City Cardiomyopathy Questionnaire score. Further, echocardiographic measurements on chronic filling pressures and whether AIR001 improves ventilator efficiency are being measured, all of which assessments will be utilized to plan further development of AIR001 in HFpEF.

After an informative NHLBI study, known as HF-ACTION, revealed supervised aerobic exercise showed a modest reduction in cardiovascular hospitalizations, mortality, and quality of life, the INABLE-TRAINING study, which is evaluating whether the combination of AIR001 and exercise training will improve exercise capacity (as measured by CPET), measures of exercise hemodynamics (measured echocardiographically) and quality of life, is expected to provide additional data to support the use of AIR001 to improve exercise capacity in patients with HFpEF.

Datasets from the ongoing Phase 2 studies, if supportive of further development of AIR001 in HFpEF patients, along with the completed toxicology studies and prior AIR001 human safety data, will be adequate for an end of Phase 2 meeting with the FDA to enter into discussion regarding a Phase 3 program in HFpEF.

AIR001 Phase 1/2 Clinical Study in Cystic Fibrosis Patients

An investigator-sponsored open-label Phase 1/2 study of nebulized inhaled AIR001 in adults with cystic fibrosis (CF) patients and airway infection with *Pseudomonas aeruginosa* (*P. aeruginosa*) was initiated in January 2017 and is being conducted at a prestigious research institution with funding from a grant award from a non-profit organization. The study will assess safety of nebulized inhaled AIR001 administered in a dose escalation manner. The study also aims to explore the effects of AIR001 on measures of lung function, exhaled airway nitric oxide, and reduction in bacterial burden. Sodium nitrite has demonstrated in vitro antimicrobial activity against *P. aeruginosa* and other airway pathogens, as well as the ability to disperse biofilms. If supportive, we believe data from this Phase 1/2 study would facilitate the design of a potential Phase 2 program to establish AIR001's utility as an antimicrobial agent for *P. aeruginosa* and sensitizer to standard antibiotic therapies in CF patients.

Vepoloxamer

Vepoloxamer (also known as MST-188) is purified poloxamer 188, a nonionic, block copolymer comprised of a central linear chain of hydrophobic polyoxypropylene flanked on both sides by linear hydrophilic polyoxyethylene chains. Vepoloxamer's mechanism of action is believed to be biophysical and driven by its ability to modulate cell membrane surface tension. We acquired the vepoloxamer program through the acquisition of privately-held SynthRx, Inc. in April 2011.

Over the past five years, we had focused our resources primarily on the clinical development of vepoloxamer, including conducting a 388-patient Phase 3 clinical study of vepoloxamer for the treatment of vaso-occlusive crisis in patients with sickle cell disease, known as the EPIC study, and smaller studies intended support a new drug application, or NDA, for vepoloxamer. More than 75 study sites in 14 countries participated in EPIC. We also were conducting a Phase 2 study of vepoloxamer for the treatment of heart failure in which we planned to enroll approximately 150 patients and had opened 10 study sites in the U.S. and Australia.

In September 2016, we announced that the Phase 3 study of vepoloxamer did not achieve its primary or secondary efficacy endpoints. Additional analyses of study data indicated that further investigation of vepoloxamer in sickle cell disease was not warranted. We determined to discontinue clinical development of vepoloxamer and wind down all clinical studies with this agent.

Vepoloxamer has demonstrated multiple pharmacologic effects that may provide clinical benefit in a wide range of diseases and conditions typically characterized by impaired microvascular blood flow and/or damaged cell membranes, but, since September 2016, we have limited our development of vepoloxamer to a nonclinical study in ischemic stroke being funded by a Small Business Innovation Research (SBIR) grant from the National Institute of Neurological Disorders and Stroke of the National Institutes of Health (NIH). That nonclinical study is evaluating the effects of vepoloxamer in combination with tissue plasminogen activator (tPA) in experimental models of embolic stroke. The study is being conducted in collaboration with leading stroke researchers at the Neuroscience Institute at Henry Ford Health System and is expected to be completed in the first quarter of 2017.

We do not plan to direct any additional capital toward the development of vepoloxamer during the next 12 months. We are exploring opportunities to monetize our vepoloxamer-related assets in order to focus our resources on AIR001's development.

Manufacturing

We do not have, and have not made plans to establish, our own manufacturing facilities. We meet our requirements for nonclinical and clinical trial material (including manufacturing API, formulating and assembling final drug product, labeling, testing and release, packaging, storing API and finished drug product and similar activities) by establishing relationships with third-party manufacturers and other service providers to perform these services for us.

In the case of AIR001 clinical trial material, we have single-source, third-party suppliers of API and finished drug product and there are a limited number of manufacturers with the technical capabilities and desire to produce AIR001. In addition, AIR001 is a liquid formulation that is administered via nebulization and the proprietary nebulizer device currently validated for use in clinical studies of AIR001 is manufactured and supplied by a single third-party, Philips Respironics, Inc.

We may investigate manufacturing-related opportunities to enhance our proprietary position around AIR001, including those involving alternative drug product formulations and delivery systems.

In the case of vepoloxamer, following the negative results from the Phase 3 clinical study, we terminated our vepoloxamer-related manufacturing and supply agreements and currently we do not have any manufacturing capabilities for vepoloxamer.

In the future, establishing supply agreements, particularly with respect to commercial manufacturing and supply, may require us to agree to substantial investment in infrastructure, minimum volume requirements, exclusivity arrangements, and/or other restrictive or potentially costly terms. Our alternatives may be limited due to the specialized nature of the technologies and methods used to manufacture our product candidates and, in the case of AIR001, the specialized and proprietary device needed for administration of our product candidate. In addition, if we seek to make certain changes to the manufacturing process, including changing our sources of API starting material, API, or finished drug product, or to the drug delivery device, we may need FDA review and approval before a change can be implemented. Among other things, the FDA may require clinical, stability or other data for any product candidate manufactured with new materials or by new manufacturers, which data will take time and is costly to generate, and the delay associated with generating this data would increase our costs and may delay completion of development of a product candidate and/or its commercial launch or, once launched, our ability to meet market demand for the product.

Intellectual Property

To protect our proprietary compounds, we have implemented and will continue to pursue a multi-faceted approach that relies on a combination of patent protection, proprietary know-how, trade secrets, and data and market exclusivity. We seek to establish and protect our proprietary rights through confidentiality, licensing and other agreements, including those with our contract manufacturers and drug delivery device supplier.

In the case of AIR001, we have filed for patent protection covering various methods of therapeutic use of inorganic nitrite, including the use of inhaled inorganic nitrite for treating HFpEF. We may also seek to obtain licenses to third party patents and other rights to the extent we determine they relate to potential therapeutic uses of AIR001. Additionally, we believe there is potential to establish exclusivity around the combination of AIR001 and its inhalation delivery system. Other medications that alter pulmonary pressures include their delivery device in their U.S. and European market labels, and are approved for use only with the specified proprietary delivery device.

In the case of vepoloxamer, we have an issued patent that includes claims covering composition of matter, methods of use, and methods of making certain purified forms of poloxamer 188, including vepoloxamer. United States Patent No. 9,403,941, "Poloxamer Composition Free of Long Circulating Material and Methods for Production and Uses Thereof" will expire no earlier than July 2035. In addition, we have four issued patents outside of the U.S. relating to methods of use of purified poloxamers to treat storage-lesioned compromised blood and compositions composed of purified poloxamers and storage-lesioned compromised blood. We have filed other vepoloxamer-related patent applications. However, in connection with our decision to terminate our vepoloxamer clinical development programs, we have abandoned certain of those patent applications and may choose to abandon additional vepoloxamer-related applications in the future.

We are aware of a substantial number of patents issued and patent applications filed in our technical areas or fields, and we may want or determine that we need to obtain licenses to patents or other rights owned by third parties. There is a risk that third parties may allege that they have patent rights encompassing our products or methods and no assurance can be given that patents do not exist, have not been filed, or could not be filed or issued, that contain claims covering our product candidates or methods.

We cannot provide assurance that our pending patent applications will issue as patents, that any issued patents will provide us with significant competitive advantages, or that the validity or enforceability of any of our patents will not be challenged or, if instituted, that these challenges will not be successful. The cost of litigation to uphold the validity and prevent infringement of our patents could be substantial. Furthermore, we cannot provide assurance that others will not independently develop similar technologies or methods, duplicate our technologies or methods, or design around the patented aspects of our products, technologies or methods. We can provide no assurance that our proposed

technologies will not infringe patents or rights owned by others, licenses to which might not be available to us.

In addition, the approval process for patent applications in different countries may differ significantly. The patent authorities in each country administer that country's laws and regulations relating to patents independently of the laws and regulations of any other country and the patents must be sought and obtained separately, which can add substantial cost and expense. Further, a favorable outcome or approval in one country does not necessarily indicate that a favorable outcome or approval will be obtained in other countries.

Competition

The industries in which we operate (biopharmaceutical, specialty pharmaceutical, biotechnology and pharmaceutical) are highly competitive and subject to rapid and significant change. We may not be able to compete successfully against organizations with competitive products, particularly large pharmaceutical companies. Many of our potential competitors have greater clinical, regulatory, manufacturing, marketing, distribution, compliance and financial resources and experience than do we.

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Over the longer term, our ability, independently or otherwise, to successfully manufacture, market, distribute and sell any approved products, expand their usage or bring additional new products to the marketplace will depend on many factors, including, but not limited to, FDA and foreign regulatory agency approval of new products and of new indications for existing products, the efficacy and safety of our products (alone and relative to other treatment options), the degree of patent or other protection afforded to particular products, and reimbursement for use of those products.

Many other organizations are developing drug products and other therapies intended to treat the same diseases and conditions for which our product candidates are in development, and the success of others may render potential application of our product candidates obsolete or noncompetitive, even prior to completion of its development.

We are not aware of any pharmacologic therapy of proven benefit for patients with HFpEF. Therapies that have demonstrated efficacy in heart failure with reduced ejection fraction (HFrEF) have thus far failed to demonstrate improved outcomes in patients with HFpEF. A couple Phase 3 studies of Novartis' LCZ696 in patients with HFpEF are underway, with estimated completion dates of May 2019 and July 2021, respectively. We are aware of other therapies under investigation in earlier stage clinical studies for the treatment of HFpEF. We also are aware of a non-surgical medical device being studied for treatment of HFpEF patients in the U.S., which device has received CE Mark approval in the European Union.

Should any therapy that receives approval prior to our product candidates become entrenched in the standard of care, the need for our product candidates may be diminished and/or such competing products may be difficult to displace. However, we believe that, as with HFrEF, there will be a need for a multimodal therapy approach to treating patients with HFpEF.

Acquisition of Aires Pharmaceuticals

We acquired our AIR001 program through the acquisition of Aires Pharmaceuticals, Inc. in February 2014. Pursuant to an agreement and plan of merger, upon completion of the acquisition, Aires became a wholly-owned subsidiary of ours. The merger consideration related to the acquisition consisted solely of shares of our common stock. All of the shares issuable to former stockholders of Aires as merger consideration were issued during 2014. There are no milestone or earn-out payments under the merger agreement. For additional information regarding the merger consideration, see "Acquisition of Aires Pharmaceuticals" under Item 7 "Management's Discussion and Analysis of Financial Condition and Results of Operations" of this report.

Acquisition of SynthRx, Inc.

We acquired our vepoloxamer program through the acquisition of SynthRx, Inc. in April 2011. Pursuant to an agreement and plan of merger, upon completion of the acquisition, SynthRx became a wholly-owned subsidiary of ours. In December 2014, we effected a roll-up of SynthRx with and into Mast Therapeutics through a short-form merger under Delaware law.

The merger consideration related to the 2011 acquisition of SynthRx consisted solely of shares of our common stock. Additional payments of up to 12,478,050 shares of our common stock to the former stockholders of SynthRx may be triggered if and when the development of vepoloxamer for the treatment of sickle cell crisis in children achieves certain milestones, specifically, the FDA's acceptance for review of an NDA covering the use of vepoloxamer for the treatment of sickle cell crisis in children and the approval of such NDA by the FDA. In light of the negative results of the Phase 3 study and our termination of clinical development of vepoloxamer in sickle cell disease, these milestones are unlikely to be achieved and we are no longer reserving shares of our common stock for their issuance.

Government Regulation

Governmental authorities in the U.S. and other countries extensively regulate the testing, manufacturing, labeling and packaging, storage, recordkeeping, advertising, promotion, import, export, marketing and distribution, among other things, of pharmaceutical products. In the U.S., the FDA, under the Federal Food, Drug and Cosmetic Act, or FDCA, and other federal statutes and regulations, subjects pharmaceutical products to rigorous review. If we do not comply with applicable requirements, we may be fined, the government may refuse to approve our marketing applications or allow us to manufacture or market our products, and we may be criminally prosecuted.

We and our third-party manufacturers, distributors and CROs may also be subject to regulations under other federal, state, and local laws, including the Occupational Safety and Health Act, the Environmental Protection Act, the Clean Air Act, the Health Insurance Portability and Accountability Act, privacy laws and import, export and customs regulations, as well as the laws and regulations of other countries.

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FDA Approval Process

To obtain approval of a new drug product from the FDA, we must, among other requirements, submit data supporting its safety and efficacy, as well as detailed information on the manufacture and composition of the drug and proposed product labeling. The testing and collection of data and the preparation of necessary applications are expensive and time-consuming. The FDA may not act quickly or favorably in reviewing these applications, and we may encounter significant difficulties or costs in our efforts to obtain FDA approvals that could delay or preclude us from marketing our product candidates.

The process required by the FDA before a new drug may be marketed in the U.S. generally involves the following:

- completion of nonclinical laboratory and animal testing performed in compliance with FDA regulations;
- submission of an investigational new drug application, or IND, which must become effective before human clinical trials may begin and must be updated annually;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the product candidate for its intended use;
- submission of an NDA after completion of pivotal clinical trials;
- a determination by the FDA within 60 days of its receipt of the NDA to file the NDA for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facilities at which the API and finished drug product are produced and tested to assess compliance with current good manufacturing practices, or cGMP;
- possible inspection of selected clinical sites to confirm compliance with good clinical practices, or GCP, requirements and data integrity; and
- FDA review and approval of the NDA prior to any commercial marketing or sale of the drug product in the U.S.

Clinical studies are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety, and the efficacy criteria to be evaluated. A protocol for each clinical study and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

The clinical investigation of an investigational new drug is generally divided into three phases that typically are conducted sequentially, but may overlap. The three phases are as follows:

• **Phase 1.** Phase 1 includes initial clinical studies introducing an investigational new drug into humans, and may be conducted in patients or normal volunteer subjects. These studies are designed to determine the metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. The number of participants included in Phase 1 studies is generally in the range of 20 to 80.

• **Phase 2.** Phase 2 includes the controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks associated with the drug. Phase 2 studies are typically well controlled, closely monitored, and conducted in a relatively small number of patients, usually involving no more than several hundred subjects.

• **Phase 3.** Phase 3 studies are typically expanded trials, which may be controlled or uncontrolled (which refers to a study that does not have a control, or comparison, group). They are performed after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather additional information about the effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling and product approval. Phase 3 studies usually are conducted at geographically dispersed clinical study sites and include from several hundred to several thousand subjects.

A clinical study may combine the elements of more than one phase and the FDA generally requires two or more Phase 3 studies to support approval of a product candidate. A company's designation of a clinical study as being of a

particular phase is not necessarily indicative that the study will be sufficient to satisfy the FDA requirements of that phase because this determination cannot

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be made until the protocol and data have been submitted to and reviewed by the FDA. In addition, a clinical study may contain elements of more than one phase notwithstanding the designation of the study as being of a particular phase.

A pivotal study is a clinical study that is believed to satisfy FDA requirements for the evaluation of a product candidate's safety and efficacy such that it can be used, alone or with other pivotal or non-pivotal studies, to justify regulatory approval. Generally, pivotal studies are Phase 3 studies, but they may be Phase 2 studies if the study design provides a well-controlled and reliable assessment of clinical benefit, particularly in an area of unmet medical need.

Clinical trials must be conducted in accordance with the FDA's good clinical practices, or GCP, requirements. The FDA may order the temporary or permanent discontinuation of a clinical study at any time or impose other sanctions if it believes that the clinical study is not being conducted in accordance with FDA requirements or that the participants are being exposed to an unacceptable health risk. An institutional review board, or IRB, generally must approve the clinical trial design and process for obtaining patient informed consent at study sites that the IRB oversees and also may halt a study, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions. Additionally, some clinical studies are overseen by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board or committee. This group recommends whether or not a trial may continue based on access to certain data from the study at designated check points.

As a product candidate moves through the clinical testing phases, manufacturing processes are further defined, refined, controlled and validated. The level of control and validation required by the FDA increases as clinical studies progress. We and the third-party manufacturers on which we rely for the manufacture of our product candidates and their respective components (including API) are subject to requirements that drugs be manufactured, packaged and labeled in conformity with cGMP. To comply with cGMP requirements, manufacturers must continue to spend time, money and effort to meet requirements relating to personnel, facilities, equipment, production and process, labeling and packaging, quality control, recordkeeping and other requirements.

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, detailed information on the product candidate is submitted to the FDA in the form of an NDA requesting approval to market the drug for one or more indications, together with payment of a significant user fee, unless waived. An NDA includes all relevant data available from pertinent nonclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information on the chemistry, manufacture, controls (CMC) and proposed labeling, among other things. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the product candidate for its intended use to the satisfaction of the FDA. In addition, under the Pediatric Research Equity Act, or PREA, an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted. However, if only one indication for a product has orphan drug designation, a pediatric assessment may still be required for any applications to market that same product for the non-orphan indication(s).

The FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. It may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. The FDA has 60 days after submission of an NDA to conduct an initial review to determine whether it is sufficient to accept for filing.

If an NDA submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the Prescription Drug User Fee Act, or PDUFA, the FDA sets a goal date by which it plans to complete its review. For a standard review, this goal date typically is 12 months from the date of submission of the NDA application. If the NDA application relates to an unmet medical need in a serious or life-threatening indication and is designated for priority review, the FDA's goal date typically is eight (8) months from the date of NDA submission. However, PDUFA goal dates are not legal mandates and FDA response often occurs several months beyond the original PDUFA goal date. Further, the review process and the target response date under PDUFA may be extended if the FDA requests, or the NDA sponsor otherwise provides, additional information or clarification regarding information already provided in the NDA. The NDA review process can, accordingly, be very lengthy. During its review of an NDA, the FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it typically follows such recommendations. Data from clinical studies are not always conclusive and the FDA and/or any advisory committee it appoints may interpret data differently than the NDA sponsor.

After the FDA evaluates the NDA and inspects manufacturing facilities where the drug product and/or its API will be produced, it will either approve commercial marketing of the drug product with prescribing information for specific indications or issue a complete response letter indicating that the application is not ready for approval and stating the conditions that must be met in

order to secure approval of the NDA. If the complete response letter requires additional data and the applicant subsequently submits that data, the FDA nevertheless may ultimately decide that the NDA does not satisfy its criteria for approval. The FDA could also approve the NDA with a Risk Evaluation and Mitigation Strategy, or REMS, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications, or a commitment to conduct post-marketing testing. Such post-marketing testing may include Phase 4 clinical studies and surveillance to further assess and monitor the product's safety and efficacy after approval. Regulatory approval of products for serious or life-threatening indications may require that participants in clinical studies be followed for long periods to determine the overall survival benefit of the drug.

If the FDA approves any of our product candidates, we will be required to comply with a number of post-approval regulatory requirements. We would be required to report, among other things, certain adverse reactions and production problems to the FDA, provide updated safety and efficacy information and comply with requirements concerning advertising and promotional labeling for any of our products. Also, quality control and manufacturing procedures must continue to conform to cGMP after approval, and the FDA periodically inspects manufacturing facilities to assess compliance with cGMP, which imposes extensive procedural, substantive and record keeping requirements. If we seek to make certain changes to an approved product, such as certain manufacturing changes, we will need FDA review and approval before the change can be implemented. For example, if we change the manufacturer of a product or its API, the FDA may require stability or other data from the new manufacturer, which data will take time and is costly to generate, and the delay associated with generating this data may cause interruptions in our ability to meet commercial demand, if any. While physicians may use products for indications that have not been approved by the FDA, we may not label or promote the product for an indication that has not been approved. Securing FDA approval for new indications is similar to the process for approval of the original indication and requires, among other things, submitting data from adequate and well-controlled studies that demonstrate the product's safety and efficacy in the new indication. Even if such studies are conducted, the FDA may not approve any change in a timely fashion, or at all.

We rely on third parties for the manufacture of our clinical trial material and we expect to rely on third-party manufacturers to produce commercial quantities of our drugs, should they receive regulatory approval in the future. Future FDA, state and/or foreign governmental agency inspections may identify compliance issues at these third-party facilities that may disrupt production or distribution or require substantial resources to correct. In addition, discovery of previously unknown problems with a product or the failure to comply with applicable requirements may result in restrictions on a product, manufacturer or holder of an approved NDA, including withdrawal or recall of the product from the market or other voluntary, FDA-initiated or judicial action that could delay or prohibit further marketing. Newly discovered or developed safety or efficacy data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. Many of the foregoing could limit the commercial value of a product or require us to commit substantial additional resources in connection with the approval of an investigational drug. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

Expedited Review Programs

Investigational drugs intended to treat serious or life-threatening conditions with unmet medical needs may be eligible for certain programs intended to expedite or facilitate the process for FDA review, such as the fast track and priority review designations. Fast track and priority review designations do not change the standards for FDA approval but may expedite the approval process.

Investigational drugs are eligible for fast track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to the combination of the drug and the specific indication for which it is being studied. For a drug with fast track designation, the FDA may consider a “rolling review” of the NDA, meaning it may agree to review sections of the NDA on a rolling basis before the complete application is submitted, which could expedite the FDA’s review of the NDA. Fast track designation, however, does not guarantee that the FDA will agree to a rolling review of the NDA. An investigational drug is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an NDA for a drug product candidate designated for priority review in an effort to facilitate the review.

Pharmaceutical Pricing and Reimbursement

Sales of our products, if approved, will depend, in part, on the extent to which the costs of our products will be covered by third-party payors, such as government healthcare programs, private health insurers, managed healthcare providers, and other organizations. These third-party payors are increasingly challenging drug prices and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. If these third-party payors do not consider our

products to be cost-effective compared to other therapies, they may not cover our products after approval as a benefit under their plans or, even if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis. In the case of products administered in an inpatient hospital setting, a level of payment that is inadequate to cover the cost to hospitals of providing and administering our products to patients, could delay acceptance of or limit our ability to penetrate the markets for our products.

Significant uncertainty exists as to the reimbursement status for newly approved drug products, including coding, coverage and payment. Sales of any products for which we obtain marketing approval will depend in part on coverage and adequate payment from third-party payors. There is no uniform policy requirement for coverage and reimbursement for drug products among third-party payors in the United States, therefore coverage and reimbursement for drug products can differ significantly from payor to payor. The coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate payment will be applied consistently or obtained. The process for determining whether a payor will cover and how much it will reimburse a product may be separate from the process of seeking approval of the product or for setting the price of the product. Even if reimbursement is provided, market acceptance of our products may be adversely affected if the amount of payment for our products proves to be unprofitable for healthcare providers or less profitable than alternative treatments or if administrative burdens make our products less desirable to use. Third-party payor reimbursement to providers of our products, if approved, may be subject to a bundled payment that also includes the procedure of administering our products. To the extent there is no separate payment for our product(s), there may be further uncertainty as to the adequacy of reimbursement amounts.

Additionally, the containment of healthcare costs has become a priority of federal and state governments and the prices of drug products have been a focus in this effort. For example, there have been several recent U.S. Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. We expect that federal, state and local governments in the U.S. will continue to consider legislation directed at lowering the total cost of healthcare. In addition, in certain foreign markets, the pricing of drug products is subject to government control and reimbursement may in some cases be unavailable or insufficient.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively referred to as the ACA, enacted in March 2010, has had and is expected to continue to have a significant impact on the healthcare industry. The ACA, among other things, imposes a significant annual fee on certain companies that manufacture or import branded prescription drug products. The ACA also increased the Medicaid rebate rate and the volume of rebated drugs has been expanded to include beneficiaries in Medicaid managed care organizations. The ACA also expanded the 340B drug discount program (excluding orphan drugs), included a 50% discount on brand name drugs for Medicare Part D participants in the coverage gap, and revised the definition of “average manufacturer price” for reporting purposes, which could increase the amount of the Medicaid drug rebates paid to states. It also contains substantial provisions intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against healthcare fraud and abuse, add new transparency requirements for the healthcare industry, impose new taxes and fees on pharmaceutical manufacturers, and impose additional health policy reforms, any or all of which may affect our business. Since its enactment there have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. Certain provisions of the ACA are not yet, or have only recently become, effective, and others have been temporarily suspended, but the ACA is likely to continue the downward pressure on pharmaceutical pricing, and may also increase our regulatory burdens and operating costs.

Other legislative changes have also been proposed and adopted since the ACA was enacted. For example, the Budget Control Act of 2011 resulted in aggregate reductions in Medicare payments to providers of up to 2% per fiscal year, which went into effect in 2013 and, following passage of the Bipartisan Budget Act of 2015, will stay in effect through 2025 unless additional Congressional action is taken. Additionally, the American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding.

It is uncertain whether and how future legislation, whether domestic or abroad, could affect prospects for our product candidates or what actions federal, state, or commercial payors for healthcare treatment and services may take in response to any such healthcare reform proposals or legislation. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures reforms may prevent or limit our ability to generate revenue, attain profitability or commercialize our product candidates.

Other Healthcare Laws and Compliance Requirements

In addition to FDA requirements, several other types of state and federal laws apply and will apply to our operations. These laws include, among others, healthcare information and data privacy protection laws, transparency laws, and fraud and abuse laws, such as anti-kickback and false claims laws.

The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item, good, facility or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exceptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor.

Federal false claims laws and civil monetary penalties laws prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. Pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly promoting their products for uses for which they were not approved and causing the submission of claims for payment for such use under federal healthcare programs. In addition, the Health Insurance Portability and Accountability Act of 1996, or HIPAA, prohibits persons and entities from knowingly and willfully executing a scheme to defraud any health care benefit program, including private payors, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for health care benefits, items or services.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, on certain types of individuals and entities, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.

The federal transparency requirements under the ACA, requires certain manufacturers of drug products, medical devices, biologics and medical supplies to annually report to the Department of Health and Human Services information related to payments and other transfers of value to physicians and teaching hospitals and physician ownership and investment interests. Compliance with such reporting requirements may be costly.

The majority of states also have statutes or regulations similar to the aforementioned federal anti-kickback and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. We may be subject to state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. In addition, we may be subject to reporting requirements under state transparency laws, as well as state laws that require pharmaceutical companies to comply with the industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government that otherwise restricts certain payments that may be made to healthcare providers and entities.

Because we intend to commercialize products that could be reimbursed under federal and other governmental healthcare programs, we plan to develop a compliance program that establishes internal controls to facilitate adherence to the rules and healthcare program requirements. Although compliance programs and adherence thereto may mitigate the risk of violation of and subsequent investigation and prosecution for violations of the laws described above, the risks cannot be eliminated entirely. In addition, due to the breadth of these laws and the narrowness of available statutory and regulatory exceptions, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If we or our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil

and criminal penalties, damages, fines, individual imprisonment, disgorgement, exclusion of products from reimbursement under U.S. federal or state healthcare programs, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings and/or the curtailment or restructuring of our operations.

Government Regulation Outside the U.S.

In addition to regulations in the U.S., we may be subject to a variety of regulations in foreign jurisdictions that govern, among other things, clinical studies and any commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product candidate, we must obtain the requisite approvals from regulatory authorities in foreign jurisdictions prior to the commencement of clinical studies or marketing and sale of the product in those countries. The foreign regulatory approval process includes all of the risks associated with the FDA approval described above. Some foreign jurisdictions have a drug product approval process similar to that in the U.S., which requires the submission of a clinical trial application much like the IND prior to the commencement of clinical studies. In Europe, for example, a clinical trial application, or CTA, must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical trial development may proceed.

To obtain regulatory approval of a product candidate under European Union regulatory systems, we would be required to submit a Marketing Authorisation Application, which is similar to the NDA, except that, among other things, there are country-specific document requirements. For countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical studies, product approval, pricing and reimbursement vary from country to country. In addition, regulatory approval of prices is required in most countries other than the U.S. We face the risk that the resulting prices would be insufficient to generate an acceptable return to us or any future partner of ours. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Research and Development Expenses

Our research and development expenses were \$20.8 million in 2016, \$28.3 million in 2015 and \$19.4 million in 2014. Our research and development expenses for all three years consisted primarily of costs associated with the Phase 3 clinical study of vepoloxamer in sickle cell disease, the Phase 2 studies of vepoloxamer in heart failure and acute limb ischemia, and research-related manufacturing for vepoloxamer and AIR001. See Item 7 “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in this report for more information regarding our research and development expenses.

Employees

As of March 2, 2017, Mast Therapeutics has nine employees, six of which are full time and three of which are temporary, part-time employees providing transitional services to us. Our employees are not unionized and we believe that our relationship with our employees is good.

Formation

Our company was incorporated in Delaware in December 1995. In October 2000, we merged our wholly-owned subsidiary, Biokeys Acquisition Corp., with and into Biokeys, Inc. and changed our name to Biokeys Pharmaceuticals, Inc. In May 2003, we merged Biokeys, Inc., a wholly-owned subsidiary, with and into us and changed our name to ADVENTRX Pharmaceuticals, Inc. In March 2013, we merged Mast Therapeutics, Inc., a wholly-owned subsidiary, with and into us and changed our name to Mast Therapeutics, Inc.

Trademarks

“Mast Therapeutics,” the Mast Therapeutics logo, “VOICE Crisis Alert,” “Aironite,” “SynthRx” and “Exelbine” are trademarks or service marks of Mast Therapeutics, Inc. or its subsidiaries. This report contains additional trademarks, services marks or trade names of others, which are the property of their respective owners. Use or display by us of other parties’ trademarks, service marks, trade names, trade dress or products is not intended to and does not imply a relationship with, or endorsements or sponsorship of, us by the trademark, service mark, trade name, trade dress or product owners.

Available Information

Our website is located at <http://www.masttherapeutics.com>. Information found on our website is not incorporated by reference into this annual report on Form 10-K. We make our filings with the U.S. Securities and Exchange Commission, or SEC, including our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and any amendments and exhibits to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, available free of charge on or through our

website, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Copies of our SEC filings are located at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Information on the operation of the Public Reference Room can be obtained by calling the SEC at 1-800-SEC-0330. In addition, the SEC maintains a website that contains reports, proxy and information statements, and other information regarding our filings at <http://www.sec.gov>.

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Item 1A. Risk Factors.

Investment in our securities involves a high degree of risk and uncertainty. Our business, operating results, growth prospects and financial condition are subject to various risks, many of which are not exclusively within our control, that may cause actual performance to differ materially from historical or projected future performance. We urge investors to consider carefully the risks described below, together with all of the information in this report and our other public filings, before making investment decisions regarding our securities. Each of these risk factors, as well as additional risks not presently known to us or that we currently deem immaterial, could adversely affect our business, operating results, growth prospects or financial condition, as well as the trading price of our common stock, in which case you may lose all or part of your investment.

Risks Related to Our Proposed Merger with Savara

The exchange ratio is not adjustable based on the market price of our common stock so the merger consideration at the closing may have a greater or lesser value than at the time we signed the merger agreement.

Our merger agreement with Savara has set the exchange ratio for the Savara common stock, and the exchange ratio is only adjustable upward or downward under certain circumstances. Any changes in the market price of our common stock before the completion of the merger will not affect the number of shares Savara securityholders will be entitled to receive pursuant to the merger agreement. Therefore, if before the completion of the merger the market price of our common stock declines from the market price on the date of the merger agreement, then Savara securityholders could receive merger consideration with substantially lower value. Similarly, if before the completion of the merger the market price of our common stock increases from the market price on the date of the merger agreement, then Savara securityholders could receive merger consideration with substantially more value for their shares of Savara capital stock than the parties had negotiated for in the establishment of the exchange ratio. Because the exchange ratio does not adjust as a result of changes in the value of our common stock, for each one percentage point that the market value of our common stock rises or declines, there is a corresponding one percentage point rise or decline, respectively, in the value of the total merger consideration issued to Savara securityholders.

Failure to complete the merger may result in Mast and Savara paying a termination fee or expenses to the other party and could harm the common stock price of Mast and future business and operations of each company.

If the merger is not completed, Mast and Savara are subject to the following risks:

- if the merger agreement is terminated under certain circumstances, we will be required to pay Savara a termination fee of \$1.8 million;
- if the merger agreement is terminated under certain circumstances, Savara will be required to pay us a termination fee of \$2.5 million;
- the price of our stock may decline and remain volatile, which may result in the delisting of our common stock from the NYSE MKT; and
- costs related to the merger, such as legal and accounting fees, and with respect to Mast, tail insurance premiums, which Mast and Savara estimate will total approximately \$2.6 million and \$1.5 million, respectively, some of which must be paid even if the merger is not completed.

In addition, if the merger agreement is terminated and our board of directors determines to seek another business combination, there can be no assurance that we will be able to find a partner willing to provide equivalent or more attractive strategic alternative than the proposed merger with Savara.

If the conditions to the merger are not met, the merger may not occur.

Even if the merger is approved by our stockholders and the stockholders of Savara, specified conditions must be satisfied or waived to complete the merger. Including, but not limited to:

- certain representations and warranties made by each party to the merger agreement must be true and correct, with the same force and effect as if made on and as of the closing date of the merger;
- there must not have been any change, occurrence or circumstance in the business, results of operations or financial condition of the parties that would prevent a party from consummating the merger or has had, individually or in the aggregate, a material adverse effect on the party's business, financial condition, operations, or result of operations;

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- the shares of our common stock to be issued to Savara securityholders in the merger must have been approved for listing on the NYSE MKT; and
- the contemplated reverse stock split must have become effective;

We cannot assure you that all of the conditions will be satisfied or waived. If the conditions are not satisfied or waived, the merger may not occur or will be delayed, and we each may lose some or all of the intended benefits of the merger.

The merger may be completed even though material adverse changes may result from the announcement of the merger, industry-wide changes and other causes.

In general, either Mast or Savara can refuse to complete the merger if there is a material adverse change affecting the other party between the date of the merger agreement, and the closing. However, certain types of changes do not permit either party to refuse to complete the merger, even if such change could be said to have a material adverse effect on Mast or Savara, including:

- any effect, change, event, circumstance or development in the conditions generally affecting the industries in which Savara and Mast operate or the United States or global economy or capital markets as a whole;
- any natural disaster or any acts of terrorism, sabotage, military action or war or any escalation of worsening thereof;
- any failure by Mast or Savara to meet internal projections or forecasts or third party revenue or earnings predictions for any period ending on or after January 6, 2017;
- any changes in GAAP or applicable legal requirements after January 6, 2017; or
- with respect to Mast, any change in the price or trading volume of our common stock.

If adverse changes occur and Mast and Savara still complete the merger, the combined organization stock price may suffer. This in turn may reduce the value of the merger to the stockholders of Mast, Savara or both.

Some Mast and Savara executive officers and directors have interests in the merger that are different from yours and that may influence them to support or approve the merger without regard to your interests.

Certain officers and directors of Mast and Savara participate in arrangements that provide them with interests in the merger that are different from yours, including, among others, the continued service as an officer or director of the combined organization, severance benefits, cash and equity bonuses contingent upon the closing of the merger, continued indemnification and the potential ability to sell an increased number of shares of common stock of the combined organization in accordance with Rule 144 under the Securities Act of 1933, as amended, or the Securities Act. For example, we previously entered into severance agreements with our executive officers that provide them with cash severance payments, cash payments intended to cover certain health insurance costs and the acceleration of their outstanding equity awards in the event their employment is terminated without cause following a change of control of our company. In addition, certain of our directors and executive officers have options and restricted stock units, or RSUs, which RSUs shall vest immediately prior to the date the merger is consummated, and our executive officers are eligible for a cash bonus award upon the closing of the merger. Two members of our board of directors are expected to continue as directors of the combined organization upon the closing of the merger, and all of our directors and executive officers are entitled to certain indemnification and liability insurance coverage pursuant to the terms of the merger agreement and coverage pursuant to our insurance policies.

Based on the terms of their respective severance agreements, outstanding equity awards and incentive awards granted in January 2017, our executive officers will be entitled to receive a total value of approximately \$2.5 million (collectively, not individually) in connection with the consummation of the merger and the associated termination of their employment from our company, based on data available as of March 2, 2017.

The market price of our common stock following the merger may decline as a result of the merger.

The market price of our common stock may decline as a result of the merger for a number of reasons including if:

- investors react negatively to the prospects of the combined organization's business and prospects from the merger;
- the effect of the merger on the combined organization's business and prospects is not consistent with the expectations of financial or industry analysts; or

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the combined organization does not achieve the perceived benefits of the merger as rapidly or to the extent anticipated by financial or industry analysts.

Our stockholders may not realize a benefit from the merger commensurate with the ownership dilution they will experience in connection with the merger.

If the combined organization is unable to realize the full strategic and financial benefits currently anticipated from the merger, our stockholders will have experienced substantial dilution of their ownership interests in our company without receiving any commensurate benefit, or only receiving part of the commensurate benefit to the extent the combined organization is able to realize only part of the strategic and financial benefits currently anticipated from the merger.

During the pendency of the merger, we may not be able to enter into a business combination with another party at a favorable price because of restrictions in the merger agreement, which could adversely affect our business.

Covenants in the merger agreement impede the ability of Mast and Savara to make acquisitions, subject to certain exceptions relating to fiduciaries duties, as set forth below, or complete other transactions that are not in the ordinary course of business pending completion of the merger. As a result, if the merger is not completed, we may be at a disadvantage to our competitors during that period. In addition, while the merger agreement is in effect, each party is generally prohibited from soliciting, initiating, encouraging or entering into certain extraordinary transactions, such as a merger, sale of assets or other business combination outside the ordinary course of business, with any third party, subject to certain exceptions described below. These restrictions apply even if such transactions could be favorable to our stockholders.

Certain provisions of the merger agreement may discourage third parties from submitting alternative takeover proposals, including proposals that may be superior to the arrangements contemplated by the merger agreement.

The terms of the merger agreement prohibit each of Mast and Savara from soliciting alternative takeover proposals or cooperating with persons making unsolicited takeover proposals, except in limited circumstances when such party's board of directors determines in good faith that an unsolicited alternative takeover proposal is or is reasonably likely to lead to a superior takeover proposal and is reasonably capable of being consummated and that failure to cooperate with the proponent of the proposal is reasonably likely to result in a breach of the board's fiduciary duties. In addition, if we or Savara terminate the Merger Agreement under certain circumstances, including terminating because of a decision of a board of directors to recommend a superior proposal, we would be required to pay a termination fee of \$1.8 million to Savara or Savara would be required to pay a termination fee of \$2.5 million to us, respectively. This termination fee may discourage third parties from submitting alternative takeover proposals to us or our stockholders, and may cause our board of directors to be less inclined to recommend an alternative proposal.

Because the lack of a public market for Savara shares makes it difficult to evaluate the fairness of the merger, the stockholders of Savara may receive consideration in the merger that is less than the fair market value of the Savara shares and/or we may pay more than the fair market value of the Savara shares.

The outstanding capital stock of Savara is privately held and is not traded in any public market. The lack of a public market makes it extremely difficult to determine the fair market value of Savara. Because the percentage of our equity to be issued to Savara securityholders was determined based on our negotiations with Savara, it is possible that the value of our common stock to be issued to Savara securityholders will be less than the fair market value of Savara, or we may pay more than the aggregate fair market value for Savara.

The exchange ratio is subject to an upward adjustment to the extent that our net cash at the effective time of the merger is less than zero dollars and as a result, our securityholders could own less of the combined company.

The exchange ratio is subject to an upward adjustment to the extent that our net cash at the effective time of the merger is less than zero dollars (\$0.00) and, as a result, our securityholders could own less, and Savara securityholders could own more, of the combined company. Certain of our outstanding warrants provide that, in the event of certain fundamental transactions, whereby a person or group of persons acquires more than 50% of our common stock, then, holders of such outstanding warrants may elect and require us to purchase the warrants held by such holder by making a cash payment in an amount equal to the Black-Scholes Value of the remaining unexercised portion of such holder's warrants. We do not believe that any cash payment is required pursuant to the terms of the warrants as a result of the merger; provided, however, that if we shall be required pursuant to the terms of the warrants to make any cash payments or otherwise settle the warrants prior to closing, the exchange ratio could be adjusted to adversely impact the ownership of our stockholders in the combined company.

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RISKS RELATED TO OUR BUSINESS

Risks Related to Our Capital Requirements, Finances and Operations

We are a clinical-stage company with no drug products approved for commercial sale, we have incurred net losses since our inception, we expect to incur substantial losses and negative operating cash flow for the foreseeable future, and we need additional funding to continue to conduct our operations and advance development of our product candidates.

We are a clinical-stage biopharmaceutical company and have not generated sustainable revenue from operations or been profitable since inception, and we may never achieve profitability. We have devoted our resources to acquiring and developing proprietary product candidates, but such product candidates cannot be marketed until clinical development is completed and governmental approvals have been obtained. None of our product candidates has been approved for sale by any regulatory agency or is available for commercial sale and each will require significant additional capital to advance their development toward regulatory approval for commercial sale.

For the years ended December 31, 2016, 2015 and 2014, we incurred losses from operations of \$36.5 million, \$39.4 million and \$29.3 million, respectively, and our net cash used in operating activities was \$37.3 million, \$32.9 million and \$24.6 million, respectively. At December 31, 2016, we had an accumulated deficit of \$311.1 million, our cash, cash equivalents and investment securities were \$11.3 million, and our working capital was \$7.3 million. We expect to continue to incur substantial operating losses for the next several years as we advance our product candidates, which are in intermediary to early stages of development, through clinical studies and other development activities necessary to seek approval from the FDA and regulatory authorities outside of the U.S. to commercialize them. Accordingly, there is no current source of revenue from operations, much less profits, to sustain our present activities. Further, no revenue from operations will likely be available until, and unless, one of our product candidates is approved by the FDA or another regulatory agency and successfully marketed, or we enter into an arrangement that provides for licensing revenue or other partnering-related funding, outcomes which we may not achieve.

We estimate that our existing capital resources are sufficient to fund our current and planned operations into the second quarter of 2017. We are focused on managing our operating expenses and maintaining adequate cash to run our business through consummation of the proposed merger with Savara. There can be no assurance that we will be successful in completing the merger with Savara or in maintaining or raising sufficient additional capital to fund continued operations.

We cannot predict the extent of our future operating losses and accumulated deficit, and we may never generate sufficient revenues to achieve or sustain profitability. To become and remain profitable, we must succeed in developing and obtaining required regulatory approvals and commercializing our product candidates. This will require us to succeed in a range of challenging activities, and many aspects of drug development are inherently unpredictable. We may never succeed in obtaining the FDA's or another regulatory authority's approval to market our product candidates or otherwise generate revenues sufficient to achieve profitability. If we do achieve profitability, we may not be able to sustain it.

There is substantial doubt as to our ability to continue as a going concern.

At December 31, 2016, our cash, cash equivalents and investment securities were \$11.3 million and our working capital was \$7.3 million. We continue to incur significant operating losses we do not believe our capital resources as of December 31, 2016 will be sufficient to fund our planned operations for the next 12 months, and we may not be able to raise additional capital as and when needed. These uncertainties raise substantial doubt regarding our ability to continue as a going concern.

As more fully discussed in Note 1 to the condensed consolidated financial statements included in this report and Part I, Item 2 “Management’s Discussion and Analysis of Financial Condition and Results of Operations” of this report, if we are unable to complete the proposed merger with Savara, we may elect to, among other things, attempt to complete another strategic transaction like the proposed merger, attempt to sell or otherwise dispose of our various assets, or continue to operate our business, focusing on advancing the development of AIR001. If our board of directors decides to dissolve our company and liquidate our assets, we would be required to pay all of our debts and contractual obligations, and to set aside certain reserves for potential future claims, and there can be no assurance as to the amount or timing of available cash left to distribute to our stockholders after paying our debts and other obligations and setting aside funds for potential future claims. If we attempt to continue to operate our business, focusing on development of AIR001, we would need to raise significant additional funds to fund our operations and execute on our business strategy and we may not be successful in those efforts.

We have historically been able to raise capital through equity offerings; however, there is no assurance that we will be successful in that regard in the future or that we will be able to obtain sufficient, or any, additional capital on acceptable terms, or at all. Further, we have based our estimated capital needs on assumptions that may prove to be wrong and we cannot assure you that estimates and assumptions will not change. For example, we are currently assuming that the investigator-sponsored clinical studies of

AIR001 we are supporting will be completed without our commitment of resources beyond what our current agreements require. If our estimated funding needs change and/or sufficient capital is not available, we may be required to further reduce the scope of, delay, or eliminate our ongoing and planned product development activities, any of which could have a material adverse effect on our business and may impair our intangible assets. In addition, we have incurred and expect to incur significant costs related to the proposed merger, such as financial advisor, legal and accounting fees, some of which must be paid even if the merger is not completed, and the extent of these costs may exceed our current estimates.

The consolidated financial statements included in this report have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. The financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from the outcome of the uncertainty related to our ability to continue as a going concern.

Our product candidates are at intermediary to early stages of development, the success of our business currently is dependent largely on our ability to advance development of AIR001 for the treatment of HFpEF, and if clinical studies of AIR001 are not successful, our business, financial condition and results of operations may be materially adversely affected and the price of our common stock may decline.

None of our product candidates has been approved for sale by any regulatory agency or is available for commercial sale. We are focusing our resources primarily on the development of AIR001. Accordingly, the success of our business currently is highly dependent on our ability, or that of a future partner, to successfully develop, obtain regulatory approval for and then successfully commercialize AIR001 and our efforts, or those of a future partner, in this regard may prove unsuccessful. Ongoing clinical studies of AIR001 may not demonstrate the safety and efficacy necessary to support continued clinical development. In addition, continued development of AIR001 will require significant additional research, formulation and manufacture development, and extensive clinical testing prior seeking regulatory approval for commercial sale and will take several years. The drug development and regulatory approval process is subject to many risks, including the risks discussed in other risk factors below, and AIR001 may never receive marketing approval from the FDA or any regulatory agency. If the results or timing of our clinical or nonclinical studies, regulatory filings, the regulatory process, regulatory developments, and other activities, actions or decisions related to AIR001 do not meet our expectations or those of securities market participants, the market price of our common stock could decline significantly. If any of our product candidates is approved by the FDA or any foreign regulatory agency, our ability to generate revenue will depend in substantial part on the extent to which that drug product is accepted by the medical community and reimbursed by third-party payors, as well as our ability to market and sell the product and ensure that our third-party manufacturers produce it in quantities sufficient to meet commercial demand, if any.

The terms of our debt facility place restrictions on our operating and financial flexibility, and failure to comply with covenants or to satisfy certain conditions of the agreement governing the debt facility may result in acceleration of our repayment obligations and foreclosure on our pledged assets, which could significantly harm our liquidity, financial condition, operating results, business and prospects and cause the price of our common stock to decline.

As of March 2, 2017, we had an outstanding principal balance of \$3.0 million under our debt facility with Hercules Capital, Inc. and Hercules Technology III, L.P. (collectively referred to as Hercules) that is secured by a lien covering substantially all of our assets, excluding intellectual property, but including proceeds from the sale, licensing or disposition of our intellectual property. The loan and security agreement governing the debt facility requires us to comply with a number of covenants (affirmative and negative), including restrictive covenants that limit our ability to: incur additional indebtedness; encumber the collateral securing the loan; acquire, own or make investments; repurchase or redeem any class of stock or other equity interest; declare or pay any cash dividend or make a cash

distribution on any class of stock or other equity interest; transfer a material portion of our assets; acquire other businesses; and merge or consolidate with or into any other organization or otherwise suffer a change in control, in each case subject to exceptions. Our intellectual property also is subject to customary negative covenants. In addition, subject to limited exceptions, Hercules could declare an event of default upon the occurrence of any event that it interprets as having a material adverse effect upon our business, operations, properties, assets, or financial condition or upon our ability to perform or pay the secured obligations under the loan and security agreement or upon the collateral or Hercules' liens on the collateral under the agreement, thereby requiring us to repay the loan immediately, together with a prepayment charge of up to 2% of the then outstanding principal balance and end-of-term charge of \$712,500, or renegotiate the terms of the agreement. Although, in and of itself, the occurrence of adverse results or delays in any clinical study or the denial, delay or limitation of approval of or taking of any other regulatory action by the FDA or another governmental entity will not constitute a material adverse effect under our loan and security agreement with Hercules, Hercules may determine that such an event together with contemporaneous events or circumstances constitutes a material adverse effect upon our business, operations, properties, assets, or financial condition or upon our ability to perform or pay the secured obligations under the loan and security agreement. If we default under the facility, Hercules may accelerate all of our repayment obligations and, if we are unable to access funds to meet those obligations or to renegotiate our agreement, Hercules could take control of our pledged assets and we could immediately cease operations. If we were to renegotiate our agreement under such circumstances, the terms may be

significantly less favorable to us. If we were liquidated, Hercules' right to repayment would be senior to the rights of our stockholders to receive any proceeds from the liquidation.

In connection with the proposed merger with Savara, because the merger would result in a change in control of our company and would otherwise trigger immediate repayment of the outstanding amount of all principal, accrued interest, accrued, unpaid fees and expenses, together with a prepayment charge of 2% of the principal balance and an end of term charge of \$712,500 (referred to as the Change in Control Prepayment Provisions), in March 2017, we entered into an amendment to our loan and security agreement with Hercules. As a result of this amendment, the proposed merger with Savara would not trigger the Change in Control Repayment Provisions and the loan would remain in place upon its existing terms, including the January 1, 2019 scheduled maturity date, following consummation of the proposed merger provided the transaction is completed on or before April 30, 2017. However, beginning on the effective date of the amendment, the terms of the agreement, as amended, will include the minimum cash requirements described below. The amendment will become effective only if and as of the date of consummation of the merger with Savara. If the amendment becomes effective, the combined company would be required to maintain (a) at least \$4 million of cash unless and until our company, Savara or the combined company raised at least \$6 million in net cash proceeds from equity and/or subordinated debt financings on or before April 30, 2017 and (b) at least \$2 million of cash unless and until our company, Savara or the combined company raised at least \$20 million in net cash proceeds from equity and/or subordinated debt financings and/or other financing sources approved by Hercules (including grant amounts) on or before August 31, 2017. The combined company's failure to comply with these requirements would be an event of default, providing Hercules with the right to require immediate repayment in full of the loan and to exercise other remedies against combined company, including those described above.

Any declaration by Hercules of an event of default could significantly harm our liquidity, financial condition, operating results, business, and prospects and cause the price of our common stock to decline.

We will need to obtain additional funding to pursue our current business strategy and continue as a going concern and we may not be able to obtain such funding on a timely basis, or on commercially reasonable terms, or at all. Any capital-raising transaction we are able to complete may result in substantial dilution to our existing stockholders, require us to relinquish significant rights, or restrict our operations.

As discussed above, based on our projected operating expenses and capital needs, our cash, cash equivalents and investment securities as of December 31, 2016, we believe that our capital resources will be sufficient to fund our operations into the second quarter of 2017, but, if the proposed merger with Savara is not completed within the timeframe we currently expect, or at all, we would need additional capital to continue operations. We may utilize our current financial resources sooner than we currently expect if we incur unanticipated expenses or the estimates and assumptions on which we have based our estimated capital needs prove to be wrong, in which case our capital resources may not be sufficient to fund operations into the second quarter of 2017.

Although we were able to raise significant funds in the past through equity financings and a debt financing, the conditions of and our access to capital markets are highly variable and adequate additional equity or debt financing may not be available to us in the future on acceptable terms, or on a timely basis, or at all. Further, each of these financing alternatives carries risks. Raising capital through the issuance of our common stock, or securities convertible into or exercisable for our common stock, may depress the market price of our stock and may substantially dilute our existing stockholders. In addition, even if we were able to raise capital through the sale and issuance of our common stock, we may not have enough authorized common stock available to raise additional capital that would be sufficient to fund planned operations for the next 12 months. As of March 2, 2017, approximately 115 million of our authorized shares of common stock were not outstanding or reserved for issuance under outstanding warrants and equity awards, equity incentive plans or other rights. Assuming a sale price of \$0.12 per share, which was the closing price of our common stock on March 2, 2017, gross proceeds from the sale of all 115 million available shares would be

approximately \$13.8 million, but any financing transaction available to us in the near-term likely would involve a sale price at a discount to market and/or significant warrant coverage. Assuming 100% warrant coverage and a sale price of \$0.12 per unit, gross proceeds from the sale of all 115 million available shares would be approximately \$6.9 million. If instead we seek to raise capital through strategic transactions, such as licensing arrangements or sales of one or more of our technologies or product candidates, we may be required to relinquish valuable rights and dilute the current and future value of our assets. For example, any licensing arrangement likely would require us to share with our licensee a significant portion of any revenues generated by our licensed technologies. Additionally, our control over the development and/or marketing of any products or product candidates licensed or sold to third parties likely would be reduced and thus we may not realize the full value of any such products or product candidates. Debt financings would likely involve covenants and/or repayment provisions that would restrict our operations. These restrictive covenants may include limitations on additional borrowing and specific restrictions on the use of our assets, including requirements to maintain specified amounts of cash or restrictions on our ability to license or sell our intellectual property assets, as well as prohibitions on our ability to create liens or make investments and may, among other things, preclude us from making distributions to stockholders (either by paying dividends or redeeming stock) and taking other actions beneficial to our stockholders. In addition, investors could impose more one-sided investment terms and conditions on companies that have or are perceived to have limited remaining funds or limited ability to raise additional funds. The lower our cash balance, the more difficult it is likely to be for us to raise additional capital on commercially reasonable terms, or at all.

Notwithstanding efforts on our part to raise additional capital, adequate additional funding may not be available on acceptable terms, or on a timely basis, or at all. We may incur significant costs in pursuing, evaluating and negotiating particular capital-raising and/or strategic or partnering transactions, even if our efforts prove unsuccessful.

We believe global economic conditions, such as volatility in the U.S. and international equity markets, may adversely impact our ability to raise additional capital. Our failure to raise capital as needed would have a material adverse effect on our financial condition and ability to pursue our business strategy and we potentially may be unable to continue as a going concern and required to liquidate our assets and dissolve our company.

If we are unable to consummate the proposed merger with Savara or raise sufficient additional capital as needed, we may be forced to delay, reduce or discontinue development of our product candidates, partner them or dispose of our assets at inopportune times or pursue less expensive but higher-risk and/or lower-return development paths.

If we are not able to consummate the proposed merger with Savara or raise sufficient additional capital as needed, we may be required to delay, reduce or discontinue one or more of our development programs, to seek collaborators or buyers at an earlier stage than otherwise would be desirable or on terms less favorable than might otherwise be available, or to liquidate our assets and dissolve our company. For example, if we do not have sufficient capital, we may determine to delay or suspend planned or ongoing clinical or nonclinical studies or other development activities and/or not to conduct other studies or activities intended to enhance our intellectual property position, improve the probability of regulatory approval, or expand the scope of a product candidate's clinical benefit and market potential. Delays in and/or reduction of development activities could impair our ability to realize the full clinical and market potential of a product candidate and have a material adverse effect on our business and financial condition. In addition, suspension or discontinuation of a development program may be viewed negatively, which could adversely affect our stock price.

To the extent we discontinue independent development of a product candidate, we may not realize any value from our investment in the discontinued program. Even if we pursue a strategic option, such as partnering, selling or exclusively licensing the program to a third party, such an option may not be available on acceptable terms or at all, and we may not realize any return on our investment in the program.

In addition, if we determine our financial resources are insufficient to fund our operations even after implementing additional cost saving measures and reducing the scope of our operations, we may be required to dispose of or liquidate our assets at values significantly less than what we believe their values to be and at which they are carried on our financial statements.

The process of developing and seeking regulatory approval of, and ultimately commercializing, investigational new drug products requires expenditure of substantial resources, and we cannot estimate with reasonable certainty the duration of or costs to complete our development programs.

Our capital requirements for the foreseeable future will depend in large part on, and could increase significantly as a result of, our expenditures on our development programs. Future expenditures on our development programs are subject to many uncertainties, and will depend on, and could increase significantly as a result of, many factors, including:

- the number, size, complexity, results and timing of our drug development programs;
- the timing and terms of any collaborative or other strategic arrangement that we may establish;
- the number of clinical and nonclinical studies necessary to demonstrate acceptable evidence of the safety and efficacy of a product candidate in a particular indication;

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the number of patients who participate, the rate of enrollment, and the ratio of randomized to evaluable patients in each clinical study;

• the number and location of sites and the rate of site initiation in each study;

• the duration of patient treatment and follow-up;

• the potential for additional safety monitoring or other post-marketing studies that may be requested by regulatory agencies;

• the time and cost to manufacture clinical trial material and commercial product, including process development and scale-up activities, and to conduct stability studies, which can last several years;

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- the degree of difficulty and cost involved in securing alternate manufacturers or suppliers of drug product, components or delivery devices, as necessary to meet FDA requirements and/or commercial demand;
- the costs, requirements, timing of, and the ability to, secure regulatory approvals;
- the extent to which we increase our workforce and the costs involved in recruiting, training and incentivizing new employees;
- the costs related to developing, acquiring and/or contracting for sales, marketing and distribution capabilities, supply chain management capabilities, and regulatory compliance capabilities, if we obtain regulatory approval for a product candidate and commercialize it without a partner;
- competing technologies and market developments; and
- the costs involved in establishing, enforcing or defending patent claims and other proprietary rights.

We may not be able to raise capital when needed or reduce other expenditures to offset expenditures on our development programs, which could have a material adverse effect on our financial condition and ability to pursue our business strategy.

Our ability to raise capital may be limited by applicable laws and regulations.

Historically, we have raised capital primarily through the sale of our equity securities. In recent years, we have raised substantial funding through equity offerings conducted under “shelf” registration statements on Form S-3. Using a shelf registration statement on Form S-3 to raise additional capital generally takes less time and is less expensive than other means, such as conducting an offering under a Form S-1 registration statement. However, our ability to raise capital using a shelf registration statement may be limited by, among other things, current SEC rules and regulations. Under current SEC rules and regulations, we must meet certain requirements to use a Form S-3 registration statement to raise capital without restriction as to the amount of the market value of securities sold thereunder. One such requirement is that the market value of our outstanding common stock held by non-affiliates, or public float, be at least \$75.0 million as of a date within 60 days prior to the date of filing the Form S-3. If we do not meet that requirement, then the aggregate market value of securities sold by us or on our behalf under the Form S-3 in any 12-month period is limited to an aggregate of one-third of our public float. Moreover, even if we meet the public float requirement at the time we file a Form S-3, SEC rules and regulations require that we periodically re-evaluate the value of our public float, and if, at a re-evaluation date, our public float is less than \$75.0 million, we would become subject to the one-third of public float limitation described above. If our ability to utilize a Form S-3 registration statement for a primary offering of our securities is limited to one-third of our public float, we may conduct such an offering pursuant to an exemption from registration under the Securities Act or under a Form S-1 registration statement, which we have done in the past, including in June 2013, and we would expect either of those alternatives to increase the cost of raising additional capital relative to utilizing a Form S-3 registration statement.

In addition, under current SEC rules and regulations, our common stock must be listed and registered on a national securities exchange in order to utilize a Form S-3 registration statement (i) for a primary offering, if our public float is not at least \$75.0 million as of a date within 60 days prior to the date of filing the Form S-3, or a re-evaluation date, whichever is later, and (ii) to register the resale of our securities by persons other than us (i.e., a resale offering). While currently our common stock is listed on the NYSE MKT equities market, there can be no assurance that we will be able to maintain such listing. The NYSE MKT reviews the appropriateness of continued listing of any issuer that falls below the exchange’s continued listing standards. For additional information regarding this risk, see the risk factor below titled “If we are unable to maintain compliance with NYSE MKT continued listing standards and policies, the NYSE MKT may commence proceedings to delist our common stock, and in some cases, determine to suspend trading in our common stock immediately without an opportunity to propose a plan that could enable us to regain compliance, which would likely cause the liquidity and market price of our common stock to decline and you could lose your investment.”

Our ability to timely raise sufficient additional capital also may be limited by the NYSE MKT's stockholder approval requirements for transactions involving the issuance of our common stock or securities convertible into our common stock. For instance, the NYSE MKT requires that we obtain stockholder approval of any transaction involving the sale, issuance or potential issuance by us of our common stock (or securities convertible into our common stock) at a price less than the greater of book or market value, which (together with sales by our officers, directors and principal stockholders) equals 20% or more of our then outstanding common stock, unless the transaction is considered a "public offering" by the NYSE MKT staff. Based on 254,746,933 shares of our common stock outstanding as of March 2, 2017 and the closing price per share of our common stock on such date, which was \$0.12, we could not raise more than approximately \$6.1 million without obtaining stockholder approval, unless the transaction is deemed a public offering or does not involve the sale, issuance or potential issuance by us of our common stock (or securities convertible into our common stock) at a price less than the greater of book or market value. In addition, certain prior sales by us may

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be aggregated with any offering we may propose in the future, further limiting the amount we could raise in any future offering that is not considered a public offering by the NYSE MKT staff and involves the sale, issuance or potential issuance by us of our common stock (or securities convertible into our common stock) at a price less than the greater of book or market value. The NYSE MKT also requires that we obtain stockholder approval if the issuance or potential issuance of additional shares will be considered by the NYSE MKT staff to result in a change of control of our company.

Obtaining stockholder approval is a costly and time-consuming process. If we are required to obtain stockholder approval for a potential transaction, we would expect to spend substantial additional money and resources. In addition, seeking stockholder approval would delay our receipt of otherwise available capital, which may materially and adversely affect our ability to execute our current business strategy, and there is no guarantee our stockholders ultimately would approve a proposed transaction. A public offering under the NYSE MKT rules typically involves broadly announcing the proposed transaction, which often times has the effect of depressing the issuer's stock price, as occurred following our issuance of a press release on February 9, 2016 announcing a proposed underwritten public offering. Accordingly, the price at which we could sell our securities in a public offering may be less, and the dilution existing stockholders experience may in turn be greater, than if we were able to raise capital through other means.

We have significant goodwill and IPR&D and impairment of goodwill and IPR&D may have a significant adverse impact on our future financial condition and results of operations.

As of December 31, 2016, we had goodwill and IPR&D of approximately \$5.5 million, representing approximately 31% of our total assets. Our intangible assets are subject to an impairment analysis whenever an event or change in circumstances indicates the carrying amount of such an asset may not be recoverable. We test our goodwill and IPR&D for impairment annually, or more frequently if an event or change in circumstances indicates that the asset may be impaired. If an impairment is identified, we would be required to record an impairment charge with respect to the impaired asset to our consolidated statements of operations and comprehensive loss. A significant impairment charge could have a material negative impact on our financial condition and results of operations.

For example, our IPR&D resulted from our acquisitions of SynthRx and Aires Pharmaceuticals in 2011 and 2014, respectively, through which we acquired our vepoloxamer and AIR001 programs, respectively. Based on our assessment of fair value of our vepoloxamer-related IPR&D as of December 31, 2016, we reduced the carrying value of our IPR&D by \$6.0 million to \$0.5 million and recorded an impairment charge of \$6.0 million as a separate operating expense in our consolidated statement of operations and comprehensive loss for the year ended December 31, 2016.

We will continue to evaluate our intangible assets for potential impairment in accordance with our accounting policies. If additional impairments are identified, we would be required to record an impairment charge with respect to the impaired asset to our consolidated statements of operations and comprehensive loss. A significant impairment charge could have a material negative impact on our financial condition and results of operations.

Events giving rise to impairment are difficult to predict and are an inherent risk in the pharmaceutical industry. Some of the potential risks that could result in impairment of our goodwill and IPR&D include negative clinical study results, adverse regulatory developments, delay or failure to obtain regulatory approval, additional development costs, changes in the manner of our use or development of vepoloxamer or AIR001, competition, earlier than expected loss of exclusivity, pricing pressures, higher operating costs, changes in tax laws, prices that third parties are willing to pay for our IPR&D or similar assets in an arm's-length transaction being less than the carrying value of our IPR&D, and other market and economic environment changes or trends. Events or changes in circumstances may lead to significant impairment charges on our goodwill and/or IPR&D in the future, which could materially adversely affect our financial condition and results of operations.

Loss of personnel, through reductions in force or otherwise, could adversely impact our ability to successfully manage our business.

We implemented significant cost-saving measures in 2016, including by restructuring our organization and reducing our workforce by more than 70%. As a result, remaining employees may have to take on substantially more responsibility, resulting in greater workload demands and potential diversion of attention away from key areas of our business. Discontinuation of the vepoloxamer clinical development programs and implementation of other cost-saving measures, including reductions in force, create uncertainty and can negatively affect staff morale, which may lead remaining employees to seek different employment. All of our employment relationships are at-will and we may lose employees not affected by reductions in force at any time if they choose to terminate their employment with us. Loss of a significant proportion of our employees and/or loss of key employees could not only serve as a distraction to remaining employees but could also cause some loss of institutional knowledge and divert significant management time and attention, which could negatively affect business strategy and execution, and our results of operations and financial condition could suffer as a result.

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Replacing key employees may be a difficult, costly and protracted process, and we may not have other personnel with the capacity to assume all of the responsibilities of a key employee upon his/her departure. Transition periods can be difficult to manage and may cause disruption to our business. In addition, there may be intense competition from other companies and organizations for qualified personnel. Other companies and organizations with which we compete for personnel may have greater financial and other resources and different risk profiles than we do, and a history of successful development and commercialization of their product candidates, which may make them more attractive employers. Our ability to compete for qualified personnel also may be adversely affected by our highly volatile stock price. The value of equity awards we may offer to candidates to induce their employment and to our employees to retain and incentivize them is significantly affected by movements in our stock price that we cannot control and may at any time be insufficient to counteract more lucrative offers from other companies. If we cannot attract and retain skilled personnel, as needed, we may not achieve our development and other goals.

In the meantime, the success of our business likely will depend in part on our ability to develop and maintain relationships with respected service providers and industry-leading consultants and advisers. If we cannot develop and maintain such relationships, as needed, the rate and success at which we can develop and commercialize product candidates may be limited. In addition, our outsourcing strategy, which has included engaging consultants that spend considerable time in our office to manage key functional areas, may subject us to scrutiny under labor laws and regulations, which may divert management time and attention and have an adverse effect on our business and financial condition.

We expend substantial resources to comply with laws and regulations relating to public companies, and any failure to maintain compliance could subject us to regulatory scrutiny and cause investors to lose confidence in our company, which could harm our business and have a material adverse effect on our stock price.

Laws and regulations affecting public companies, including provisions of the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010 and the Sarbanes-Oxley Act of 2002, or SOX, and the related rules and regulations adopted by the SEC and by the NYSE MKT have resulted in, and will continue to result in, significant costs to us as we evaluate the implications of these rules and respond to their requirements. For example, compliance with Section 404 of SOX, including performing the system and process documentation and evaluation necessary to issue our annual report on the effectiveness of our internal control over financial reporting and, if applicable, obtain the required attestation report from our independent registered public accounting firm, requires us to incur substantial expense and expend significant management time. Further, we have in the past discovered, and may in the future discover, areas of internal controls that need improvement. If we identify deficiencies in our internal controls that are deemed to be material weaknesses, we could become subject to scrutiny by regulatory authorities and lose investor confidence in the accuracy and completeness of our financial reports, which could have a material adverse effect on our stock price. Internal control over financial reporting cannot provide absolute assurance of achieving financial reporting objectives because of its inherent limitations, including the possibility of human error and circumvention by collusion or overriding of controls. Accordingly, even an effective internal control system may not prevent or detect material misstatements on a timely basis, or at all. Also, previously effective controls may become inadequate over time as a result of changes in our business or operating structure, and we may fail to take measures to evaluate the adequacy of and update these controls, as necessary, which could lead to a material misstatement. For example, loss of staff and other resources in our accounting department as a result of cost-saving measures or otherwise, could negatively impact our ability to maintain adequate internal control over financial reporting and/or disclosure controls and procedures and the accuracy and timeliness of our financial reporting. Consequently, investor confidence in our financial reports may be adversely affected, which could negatively impact our stock price.

In addition, new laws and regulations could make it more difficult or more expensive for us to obtain certain types of insurance, including director and officer liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the coverage that is the same or similar to our current coverage.

The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or board committees, and as our executive officers. We cannot predict or estimate with any reasonable accuracy the total amount or timing of the costs we may incur to comply with these laws and regulations.

Our ability to use net operating loss carry forwards and research and development tax credits to offset future taxable income or future tax will be limited, and may be limited further in the future, due to changes in ownership (within the meaning of IRC Section 382) that have occurred and may occur in the future, including as a result of the proposed merger with Savara.

In general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or IRC, a corporation that undergoes an “ownership change” is subject to limitations on its ability to utilize its pre-change net operating losses, or NOLs, and certain other tax assets to offset future taxable income, and an ownership change is generally defined as a cumulative change of 50% or more in the ownership positions of certain stockholders during a rolling three-year period. In 2012, we had identified an ownership change within the meaning of IRC Section 382 that occurred on November 11, 2011 as a result of an equity financing we completed on that date and, consequently, we do not expect to be eligible to utilize the NOL carry forwards and research and development tax credits we had accumulated as of November 11, 2011. We completed a formal study to determine if any ownership changes within

the meaning of IRC Section 382 had occurred during the years ended December 31, 2012, 2013 and 2014. None were identified. However, other ownership changes within the meaning of IRC Section 382 may occur in the future or may already have occurred in connection with the public offering of our common stock and warrants completed in February 2016, which could eliminate or restrict our ability to use NOL carry forwards and research and development tax credits generated after November 11, 2011.

In addition, the proposed merger with Savara likely will result in an ownership change for our company under Sections 382 and 383 of the IRC. Accordingly, our pre-merger NOL carryforwards and certain other tax attributes would be subject to limitations on their use after the merger. The NOL carryforwards and certain other tax attributes of Savara and of the combined company may also be subject to limitations on their use after the merger if the merger also results in an ownership change for Savara.

Limitations on our ability to use NOL carry forwards and research and development tax credits to offset future taxable income could require us to pay U.S. federal income taxes earlier than would be required if such limitations were not in effect. Similar rules and limitations may apply for state income tax purposes.

Our business and operations would suffer in the event of computer system failures, cyber-attacks on our systems or deficiency in our cyber security.

Despite the implementation of security measures, our internal computer systems, and those of third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, malware, natural disasters, fire, terrorism, war and telecommunication, electrical failures, cyber-attacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. In addition, our systems or those of third parties on which we rely safeguard important confidential personal data regarding our employees and patients enrolled in our clinical trials. If a disruption event were to occur and cause interruptions in our operations, it could result in a disruption of our drug development programs. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials 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 inappropriate disclosure of confidential or proprietary information, we could incur liability and development of our product candidates could be delayed.

Our employees, independent contractors and consultants, principal investigators, CROs, CMOs and other vendors, and any future commercial partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk that our employees, independent contractors and consultants, principal investigators, CROs, CMOs and other vendors, and any future commercial partners may engage in fraudulent conduct or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, to provide accurate information to the FDA or comparable foreign regulatory authorities, to comply with manufacturing standards required by cGMP or that we establish, to comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, and to report financial information or data accurately or disclose unauthorized activities to us. The misconduct of our employees and others we engage to provide services to us could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We maintain a code of business conduct and ethics for our directors, officers and employees, but it is not always possible to identify and deter such misconduct, and the precautions we

take to detect and prevent this activity may not be effective 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 be in compliance with such 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 and results of operations, including the imposition of significant fines or other sanctions.

Our operations might be interrupted by the occurrence of a natural disaster or other catastrophic event.

Our corporate headquarters are located in a single commercial facility in San Diego, California. Important documents and records, including copies of our regulatory documents and other records for our product candidates, are located at our facilities and we depend on our facilities for the continued operation of our business. Natural disasters and other catastrophic events, such as wildfires and other fires, earthquakes and extended power interruptions, which have impacted San Diego businesses in the past, and terrorist attacks or severe weather conditions, could significantly disrupt our operations and result in additional, unplanned expense. As a small company with limited resources, we have not prepared or implemented a formal business continuity or disaster recovery plan and any natural disaster or catastrophic event could disrupt our business operations and result in setbacks to our development programs. Even

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though we believe we carry commercially reasonable insurance, we might suffer losses that are not covered by or exceed the coverage available under these insurance policies.

Risks Related to Drug Development and Commercialization

We depend on the successful completion of clinical studies of our product candidates and positive results in prior clinical studies do not ensure that ongoing or future clinical studies will be successful.

Human pharmaceutical products generally are subject to rigorous nonclinical testing and clinical studies and other approval procedures mandated by the FDA and foreign regulatory authorities. Before obtaining regulatory approval for the commercial sale of a product candidate, we must demonstrate through additional clinical studies that the drug product is safe and effective for use in the target indication.

Clinical studies are expensive, difficult to design and implement, can take many years to complete, and outcomes are inherently uncertain. A drug product may fail to demonstrate positive results at any stage of testing despite having progressed satisfactorily through nonclinical testing and initial clinical studies. In addition, interim results of a clinical study do not necessarily predict final results. Further, clinical study data frequently are susceptible to varying interpretations. Medical professionals and/or regulatory authorities may analyze or weigh study data differently than we do, resulting in delay or failure to obtain marketing approval for a product candidate.

If we license rights to develop our product candidates to independent third parties or otherwise permit such third parties to evaluate our product candidates in clinical studies, we may have limited control over those clinical studies. For example, AIR001 is being evaluated in investigator-sponsored clinical studies over which we have limited or no control over the study design or implementation and we cannot provide assurance that any of those studies will be completed on anticipated timelines or at all. Any safety or efficacy concern identified in a third-party sponsored study could adversely affect our or another licensee's development of our product candidate and prospects for its regulatory approval, even if the data from that study are susceptible to varying interpretations and analyses.

There is significant risk that ongoing and future clinical studies of our product candidates are unsuccessful. Negative or inconclusive results could cause the FDA and other regulatory authorities to require that we repeat or conduct additional clinical studies, which could significantly increase the time and expense associated with development of that product candidate or cause us to elect to discontinue one or more clinical programs. For example, in September 2016, we announced that our Phase 3 clinical study of vepoloxamer in sickle cell disease did not achieve its primary or secondary efficacy endpoints. Shortly thereafter and as a result, we decided to discontinue our clinical development programs for vepoloxamer in sickle cell disease and heart failure. Failure to complete a clinical study of a product candidate or an unsuccessful completion of a clinical study of a product candidate could have a material adverse effect on our business and/or stock price.

All ongoing and currently planned clinical studies of our lead product candidate, AIR001, are investigator-sponsored studies over which we have limited or no control.

AIR001 is our lead product candidate and is being evaluated in multiple, investigator-sponsored Phase 2 clinical studies for the treatment of patients with HFpEF. As a result, we believe our capital requirements for advancing development of AIR001 in HFpEF are significantly less than if we were to conduct this Phase 2 clinical testing ourselves. However, because we are not the sponsor of these studies, we have limited or no control over the study design or execution, including whether the study will enroll a sufficient number of subjects or be completed on schedule, if at all. As a result, successful completion of these studies is largely outside of our control.

Delays in commencement and completion of clinical studies are common and have many causes. Delays in clinical studies of our product candidates could increase overall development costs and jeopardize our ability to obtain regulatory approval and successfully commercialize any approved products.

Clinical testing typically is expensive, can take many years to complete, and its outcome is inherently uncertain. Clinical studies may not commence on time or be completed on schedule, if at all. The commencement and completion of clinical studies can be delayed for a variety of reasons, including:

- inability to raise sufficient funding, if necessary, to initiate or continue a clinical study;
- delays in obtaining regulatory approval to commence a clinical study;

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- delays in identifying and reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical study sites and investigators, which agreements can be subject to extensive negotiation and may vary significantly among study sites;
- delays in obtaining institutional review board, or IRB, approval to conduct a clinical study at a prospective site;
- delays in reaching agreements on acceptable terms with prospective contract manufacturing organizations, or CMOs, or other vendors for the production and supply of clinical trial material and, if necessary, drug administration devices, which agreements can be subject to extensive negotiation;
- delays in the production and/or delivery of sufficient quantities of clinical trial material or drug administration devices from our CMOs and other vendors to initiate or continue a clinical study;
- delays on the part of our CROs, CMOs, and other third-party contractors in developing procedures and protocols or otherwise conducting activities in accordance with applicable policies and procedures and in accordance with agreed upon timelines;
- delays in identifying and hiring or engaging, as applicable, additional employees or consultants to assist in managing clinical study-related activities;
- delays in recruiting and enrolling individuals to participate in a clinical study;
- delays caused by subjects dropping out of a clinical study due to side effects, difficulties in adhering to the study protocol, or otherwise;
- delays in having subjects complete participation in a clinical study, including returning for post-treatment follow-up;
- delays resulting from study sites dropping out of a trial or providing inadequate staff support for the study;
- our suspension of enrollment at a study site or the imposition of a clinical hold by the FDA or other regulatory authority following an inspection of clinical study operations at study sites or finding of a drug-related serious adverse event; and
- delays in quality control/quality assurance procedures necessary for study database lock and analysis of unblinded data.

Patient enrollment, a critical component to successful completion of a clinical study, is affected by many factors, including the size and nature of the study subject population, the proximity of patients to clinical sites, the eligibility criteria for the study, the design of the clinical study, competing clinical studies and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to available alternatives, including therapies being investigated by other companies. Further, completion of a clinical study and/or its results may be adversely affected by failure to retain subjects who enroll in a study but withdraw due to adverse side effects, perceived lack of efficacy, improvement in condition before treatment has been completed, or for personal issues or by subjects who fail to return for or complete post-treatment follow-up.

Clinical studies may not begin on time or be completed in the timeframes we anticipate and may be more costly than we anticipate for a variety of reasons, including one or more of those described above. The length of time necessary to complete clinical studies varies significantly and is difficult to predict accurately. We may make statements regarding anticipated timing for completion of enrollment in and/or availability of results from our clinical studies, but such predictions are subject to a number of significant assumptions and actual timing may differ materially for a variety of reasons, including patient enrollment rates, length of time needed to prepare raw study data for analysis and then to review and analyze it, and other factors described above. In addition, in the case of AIR001, we are supporting but are not sponsoring the ongoing Phase 2 clinical studies and, as a result, the continuation and completion of and receipt of data from those studies may be largely outside of our control. If we experience delays in the completion of a clinical study, if a clinical study is terminated, or if failure to conduct a study in accordance with regulatory requirements or the study's protocol leads to deficient safety and/or efficacy data, the regulatory approval and/or commercial prospects for our product candidate may be harmed and our ability to generate product revenue will be delayed. In addition, any delays in completing our clinical studies likely will increase our development costs. Further, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical studies may ultimately lead to the denial of regulatory approval of a product candidate. Even if we are able to ultimately commercialize our product candidates, other therapies for the same indications may be introduced to the market in the

interim and establish a competitive advantage or diminish the need for our products.

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Clinical studies are very expensive, difficult to design and implement, often take many years to complete, and the outcome is inherently uncertain.

Clinical development of pharmaceutical products for humans generally is very expensive, takes many years to complete and failure can occur at any stage of clinical testing. We estimate that clinical development of our product candidates will take several additional years to complete, but because of the variety of factors that can affect the design, timing and outcome of clinical studies, we are unable to estimate the actual funds required to complete research and development and commercialize our product candidates. We will need significant additional capital to continue to advance AIR001 for the treatment of HFpEF.

Failure at every stage of clinical testing is not uncommon and we may encounter problems that would require additional, unplanned studies or cause us to abandon a clinical development program. For example, we determined to discontinue clinical development of vepoloxamer in sickle cell disease based upon the top-line results of the Phase 3 study of vepoloxamer in sickle cell disease. If results of ongoing investigator-sponsored clinical studies of AIR001 in HFpEF are negative or inconclusive, we may determine not to pursue additional clinical studies in HFpEF or any other indication.

In addition, a clinical study may be suspended or terminated by us, an IRB, a data safety monitoring board, the FDA or other regulatory authorities due to a number of factors, including:

- lack of adequate funding to continue the study;
- failure to conduct the study in accordance with regulatory requirements or the study's protocol;
- inspection of clinical study operations or sites by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;
- unforeseen safety issues, including adverse side effects; or
- changes in governmental regulations or administrative actions.

Changes in governmental regulations and guidance relating to clinical studies may occur and we may need to amend study protocols to reflect these changes, or we may amend study protocols for other reasons. Amendments may require us to resubmit protocols to IRBs for reexamination or renegotiate terms with CROs, study sites and investigators, all of which may adversely impact the costs or timing of or our ability to successfully complete a trial.

There is significant uncertainty regarding the regulatory approval process for any investigational new drug, substantial further testing and validation of our product candidates and related manufacturing processes are required, and regulatory approval may be conditioned, delayed or denied, which could delay or prevent us from successfully marketing our product candidates and substantially harm our business.

Human pharmaceutical products generally are subject to rigorous nonclinical testing and clinical studies and other approval procedures mandated by the FDA and foreign regulatory authorities. Various federal and foreign statutes and regulations also govern or influence the manufacturing, safety, labeling, storage, record keeping and marketing of pharmaceutical products. The process of obtaining these approvals and the subsequent compliance with appropriate U.S. and foreign statutes and regulations is time-consuming and requires the expenditure of substantial resources.

We expect our MAST platform to accelerate development of vepoloxamer as compared to other new molecular entities for therapeutic use in humans. For example, we consider vepoloxamer "Phase 2 ready" for clinical development in ischemic stroke. However, this expectation is predicated on the belief that regulatory authorities, such as the FDA, will consider clinical and nonclinical studies of vepoloxamer and poloxamer 188 conducted by prior sponsors and/or conducted in other diseases or conditions supportive of clinical development of vepoloxamer in stroke, which may not be the case for a variety of reasons. If regulatory agencies take the position that prior-sponsor studies of vepoloxamer and poloxamer 188 do not support the safety and efficacy of our vepoloxamer-based product candidates, they may

require additional testing of our product candidates prior to allowing us to proceed with proposed clinical studies or ultimately prior to granting marketing approval, which could require us to expend substantial additional resources and significantly extend the timeline for clinical development of vepoloxamer in stroke.

Significant uncertainty exists with respect to the regulatory approval process for any investigational new drug, including our lead product candidate, AIR001. Regardless of guidance the FDA may give a drug's sponsor during its development, the FDA retains complete discretion in deciding whether to accept a NDA for filing or, if accepted, approve an NDA. There are many components to a new drug application (NDA) submission in addition to clinical study data. For example, the FDA will review our internal systems and processes, as well as those of our CROs, CMOs and other vendors, related to development of our product candidate, including those

pertaining to our clinical studies and manufacturing processes. Before accepting an NDA for review or before approving the NDA, the FDA may request that we provide additional information that may require significant resources and time to generate and there is no guarantee that our product candidate will be approved for any indication for which we may apply. The FDA may choose not to approve an NDA for any of a variety of reasons, including a decision related to the safety or efficacy data, manufacturing controls or systems, or for any other issues that the agency may identify related to the development of our product candidate. Even if one or more Phase 3 clinical studies are successful in providing statistically significant evidence of the efficacy and safety of the investigational drug, the FDA may not consider efficacy and safety data from the submitted studies adequate scientific support for a conclusion of effectiveness and/or safety and may require an additional Phase 3 or other studies prior to granting marketing approval. If this were to occur, the overall development cost for the product candidate would be substantially greater and our competitors may bring products to market before us, which could impair our ability to generate revenues from the product and have a material adverse effect our business, financial condition and results of operations.

Further, development of our product candidates and/or regulatory approval may be delayed for reasons beyond our control. For example, U.S. federal government shut-down or budget sequestration, such as occurred during 2013, may result in significant reductions to the FDA's budget and operations, which may lead to slower response times and longer review periods, potentially affecting our ability to progress development of or obtain regulatory approval for our product candidates.

Even if the FDA grants approval, the conditions or scope of the approval may limit successful commercialization of the product and impair our ability to generate substantial sales revenue. For example, the FDA may not approve the labeling claims for our products that we request and believe are necessary or desirable for successful commercialization, or may grant marketing approval contingent on the performance of costly post-approval clinical trials or subject to warnings or contraindications. Additionally, even after granting approval, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for our products will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, and continued compliance with current good manufacturing processes, or cGMP, good clinical practices, international conference on harmonization regulations and good laboratory practices, which are regulations and guidelines that are enforced by the FDA for all of our clinical development and for any clinical studies that we conduct post-approval. The FDA may decide to withdraw approval, add warnings or narrow the approved indications in the product label, or establish risk management programs that could restrict distribution of our products. These actions could result from, among other things, safety concerns, including unexpected side effects or drug-drug interaction problems, or concerns over misuse of a product. If any of these actions were to occur following approval, we may have to discontinue commercialization of the product, limit our sales and marketing efforts, and/or conduct post-approval studies, which in turn could result in significant expense and delay or limit our ability to generate sales revenues.

We do not have, and do not have plans to establish, any manufacturing facilities and are dependent on third parties for the manufacture and supply of our clinical trial materials, and the loss of any of these vendors or their failure to provide us with an adequate supply of clinical trial material in a timely manner and on commercially acceptable terms, or at all, could harm our business.

We do not have, and do not have plans to establish, our own manufacturing facilities. For clinical trial material, we entered into supply agreements with third parties for both API and finished drug product, but our agreements may not cover all of our clinical trial material needs and we may need to negotiate new or amended agreements with these CMOs and other vendors or rely on individual proposals or statements of work, which inherently involves uncertainty as to ongoing supply and may result in delays in the completion of ongoing clinical studies or initiation of new studies. In addition, as development of our product candidates progress, we will need to negotiate agreements for commercial supply; however, we may not be able to reach agreement on acceptable terms. If we fail to maintain

relationships with our current CMOs and other vendors, we may not be able to complete development of our product candidates, or market them, if approved, on a timely basis, or at all, which would have a material and adverse effect on our business.

In addition, in connection with terminating our clinical development of vepoloxamer, we also terminated our agreements with our vepoloxamer-related CMOs and other vendors. Consequently, if we were to restart clinical development of vepoloxamer, we would have to establish new CMO relationships and may not be able to do so on a timely basis, or at all.

Third-party manufacturers and suppliers may not perform as agreed or may terminate their agreements with us. For example, because these third parties provide manufacturing services to a number of other pharmaceutical companies, they may experience capacity constraints or choose to prioritize one or more of their other customers over us. Any significant problem that our manufacturers or suppliers experience could delay or interrupt our supply of clinical trial material or commercial product until the manufacturer or supplier cures the problem or until we locate, negotiate for and validate an alternative source of supply, if one is available.

In addition to our reliance on third parties to manufacture clinical trial material, we rely on them to conduct or assist us in conducting key manufacturing development activities, including qualification of equipment, developing and validating methods,

defining critical process parameters, releasing component materials and conducting stability testing, among other things. If these third parties are unable to perform successfully in a timely manner, whether for technical, financial or other reasons, we may be unable to secure clinical trial material, which likely would delay the initiation, conduct or completion of our clinical studies, which, in turn, likely would have a material and adverse effect on our business.

All manufacturers of our clinical trial material and, as applicable, commercial product, including API manufacturers, must comply with cGMP requirements enforced by the FDA through its facilities inspection program and applicable requirements of foreign regulatory authorities. These requirements include quality control, quality assurance and the maintenance of records and documentation. Manufacturers of our clinical trial material may be unable to comply with these cGMP requirements and with other FDA, state and foreign regulatory requirements. While we or our representatives generally monitor and audit our manufacturers' systems, we have little control over their ongoing compliance with these regulations. Failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall, or withdrawal of product approval.

Currently, we do not have alternative sources to backup our primary sources of clinical trial material. Identification of and discussions with other vendors may be protracted and/or unsuccessful. Therefore, if our primary sources become unable or unwilling to perform, we could experience protracted delays or interruptions in the supply of clinical trial material and, ultimately, product for commercial sale, which could materially and adversely affect our development programs, commercial activities, operating results and financial condition. In addition, the FDA may require that we have an alternate manufacturer of a drug product before approving it for marketing and sale in the U.S. and securing such alternate manufacturer before approval of an NDA could result in considerable additional time and cost prior to NDA approval.

Any new manufacturer or supplier of finished drug product or its component materials, including API, would be required to qualify under applicable regulatory requirements and would need to have sufficient rights under applicable intellectual property laws to the method of manufacturing such product or ingredients. The FDA may require us to conduct additional clinical studies, collect stability data and provide additional information concerning any new supplier, or change in a validated manufacturing process, including scaling-up production, before we could distribute products from that manufacturer or supplier or revised process. For example, if we were to engage a third party other than our current CMOs to supply drug product for future clinical trial material or commercial product, the FDA may require us to conduct additional clinical and nonclinical studies to ensure comparability of the drug substance manufactured by our current CMOs to drug substance manufactured by the new supplier. In addition to the potential for such requirements to result in significant interruption to development and commercialization of our product candidates, we likely would incur substantial additional costs to comply with the additional requirements.

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling-up initial production. These problems include difficulties with production costs and yields, quality control, including stability of the product candidate and quality assurance testing, and shortages of qualified personnel. None of our product candidates has been manufactured at the scale we believe will be necessary to maximize its commercial value and, accordingly, we may encounter difficulties in attempting to scale-up production and may not succeed in that effort on a timely basis or at all, including as a result of delaying activities necessary to establish commercial-scale production due to capital constraints. In addition, the FDA or other regulatory authorities may impose additional requirements as we scale-up initial production capabilities, which may delay our scale-up activities or add expense.

If our manufacturers encounter any of these difficulties or otherwise fail to comply with their contractual obligations or we delay in entering into commercial supply agreements due to capital constraints, we may have insufficient

quantities of material to support ongoing and/or planned clinical studies or to meet commercial demand, if approved. In addition, any delay or interruption in the supply of materials necessary or useful to manufacture our product candidates could delay the completion of our clinical studies, increase the costs associated with our development programs and, depending upon the period of delay, require us to commence new clinical studies at significant additional expense or terminate the studies completely. Delays or interruptions in the supply of commercial product could result in increased cost of goods sold and lost sales. We cannot provide assurance that manufacturing or quality control problems will not arise in connection with the manufacture of our clinical trial material or commercial product, if approved, or that third-party manufacturers will be able to maintain the necessary governmental licenses and approvals to continue manufacturing such clinical trial material or commercial product, as applicable. In addition, vepoloxamer currently is manufactured outside the U.S. and, as a result, we may experience interruptions in supply due to shipping or customs difficulties or regional instability. Any of the above factors could cause us to delay or suspend anticipated or ongoing trials, regulatory submissions or commercialization of our product candidates, entail higher costs or result in our being unable to effectively commercialize our products. Our dependence upon third parties for the manufacture of our clinical trial material may adversely affect our future costs and our ability to develop and commercialize our product candidates on a timely and competitive basis.

We rely significantly on third parties to conduct our nonclinical testing and clinical studies and other aspects of our development programs and if those third parties do not satisfactorily perform their contractual obligations or meet anticipated deadlines, the development of our product candidates could be adversely affected.

We do not employ personnel or possess the facilities necessary to conduct many of the activities associated with our programs. We engage consultants, advisors, CROs, CMOs and others to assist in the design and conduct of nonclinical and clinical studies of our product candidates, with interpretation of the results of those studies and with regulatory activities, and we expect to continue to outsource a significant amount of such activities. As a result, many important aspects of our development programs are and will continue to be outside our direct control, and our third-party service providers may not perform as required or expected. Further, such third parties may not be as committed to the success of our programs as employees and, therefore, may not devote the same time, thoughtfulness or creativity to completing projects or problem-solving as would an employee. To the extent we are unable to successfully manage the performance of third-party service providers, our business may be adversely affected.

The CROs that we engage to execute our clinical studies play a significant role in the conduct of the studies, including the collection and analysis of study data, and we likely will depend on CROs and clinical investigators to conduct future clinical studies and to assist in analyzing data from completed studies and developing regulatory strategies for our product candidates. Individuals working at the CROs with which we contract, as well as investigators at the sites at which our studies are conducted, are not our employees, and we have limited control over the amount or timing of resources that they devote to our programs. As discussed above, with respect to our AIR001 program, because we are not the sponsor of the ongoing clinical studies of AIR001, our control over these studies is further limited. If our CROs, study investigators, and/or third-party sponsors fail to devote sufficient time and resources to studies of our product candidates, if they do not comply with all regulatory and contractual requirements, or if their performance is substandard, it may delay commencement and/or completion of these studies, submission of applications for regulatory approval, regulatory approval, and commercialization of our product candidates. Failure of CROs to meet their obligations to us could adversely affect development of our product candidates. For example, in 2006, we engaged a CRO to assist with the primary conduct of our bioequivalence study of Exelbine, including monitoring participating clinical sites to ensure compliance with regulatory requirements. FDA guidance recommends that clinical sites randomly select and retain reserve samples of study drugs used in bioequivalence studies. However, the clinical sites that participated in our bioequivalence study of Exelbine failed to do so. In August 2011, we received a complete response letter from the FDA stating that the authenticity of the study drugs used in that bioequivalence study could not be verified and, consequently, the study would need to be repeated to address that deficiency.

In addition, CROs we engage may have relationships with other commercial entities, some of which may compete with us. If they assist our competitors at our expense, it could harm our competitive position. Moreover, if a CRO fails to perform during a clinical study, we may not be able to enter into arrangements with alternative CROs on acceptable terms or in a timely manner, or at all. Switching CROs may increase costs and divert management time and attention. In addition, there likely would be a transition period when a new CRO commences work. These challenges could result in delays in the commencement or completion of our clinical studies, which could materially impact our ability to meet our desired development timelines and have a material adverse impact on our business and financial condition.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their clinical development, regulatory approval or commercialization.

Undesirable side effects caused by our product candidates could interrupt, delay or halt clinical studies and could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all indications, and in turn prevent us from commercializing our product candidates.

If any of our product candidates receive marketing approval and we or others later identify undesirable side effects caused by the product or, if applicable, the reference product:

- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- regulatory authorities may withdraw their approval of the product;
- we may be required to change the way the product is administered, conduct additional clinical studies or change the labeling of the product; and
- our reputation may suffer.

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Any of these events could prevent us from achieving or maintaining market acceptance of the affected product or could substantially increase the costs and expenses of commercializing the product, which in turn could delay or prevent us from generating significant revenue from its sale.

We may not achieve our projected development goals in the time frames we announce.

We set goals for and make public statements regarding our estimates of the timing for accomplishing certain objectives material to successful development of our product candidates. The actual timing of these events can vary, sometimes dramatically, due to many factors, including delays or failures in our nonclinical testing, clinical studies and manufacturing and regulatory activities and the uncertainties inherent in the regulatory approval process. From time to time we provide estimates for the completion of enrollment of or announcement of data from clinical studies of our product candidates. However, predicting the rate of enrollment or the time from completion of enrollment to announcement of data for any clinical study requires us to make a number of significant assumptions that may prove to be incorrect. In addition, for studies sponsored by independent third parties, we have even less control over whether the study meets anticipated timelines. If, as a clinical study progresses, we gain reliable information that materially impacts our assumptions, we will adjust our estimates. Even so, as discussed in other risk factors above, our estimated enrollment rates and the actual rates may differ materially and the time required to complete enrollment of any clinical study may be considerably longer than we estimate. In addition, even if we complete enrollment as expected, it may take longer than anticipated to prepare the data for review and then to review, analyze and announce the data, as was the case with our Phase 3 study of vepoloxamer in sickle cell disease. Such delays may adversely affect our financial condition and results of operations.

Even if we complete a clinical study with successful results, we may not achieve our projected development goals in the time frames we initially anticipate or announce. If a development plan for a product candidate becomes more extensive and costly than anticipated, we may determine that the associated time and cost are not financially justifiable and, as a result, discontinue development in a particular indication or of the product candidate as a whole. Any such action may be viewed negatively, which could adversely affect our stock price.

In addition, changes may occur in regulatory requirements or policy during the period of product development and/or regulatory review of an NDA that relate to the data required to be included in NDAs. A change in regulatory policy that is not formalized or publicly announced may result in our submission of an NDA that the FDA or a foreign regulatory agency deems insufficient to support product approval, which could substantially increase the time and cost associated with seeking regulatory approval of a product candidate.

Throughout development, we must provide adequate assurance to the FDA and other regulatory authorities that we can consistently produce our product candidates in conformance with cGMP and other regulatory standards. As discussed above, we rely on CMOs for the manufacture of clinical, and future commercial, quantities of our product candidates. If future FDA or other regulatory authority inspections identify cGMP compliance issues at these third-party facilities, production of our clinical trial material or, in the future, commercial product, could be disrupted, causing potentially substantial delay in development or commercialization of our product candidates.

Even if we receive regulatory approval for a product candidate, we may face development and regulatory difficulties that could materially and adversely affect our business, financial condition and results of operations and cause our stock price to decline.

Even if initial regulatory approval is obtained, or as a condition to the initial approval, the FDA or a foreign regulatory agency may impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies or marketing surveillance programs, any of which would limit the commercial potential of the product. Our product candidates also will be subject to ongoing FDA requirements related

to the manufacturing processes, labeling, packaging, storage, distribution, advertising, promotion, record-keeping and submission of safety and other post-market information regarding the product. For instance, the FDA may require changes to approved drug labels, require post-approval clinical studies and impose distribution and use restrictions on certain drug products. In addition, approved products, manufacturers and manufacturers' facilities are subject to continuing regulatory review and periodic inspections. If previously unknown problems with a product are discovered, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, the FDA may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we or a CMO of ours fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters or untitled letters;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approval;

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- suspend or terminate any ongoing clinical studies;
- refuse to approve pending applications or supplements to approved applications;
- exclude our product from reimbursement under government healthcare programs, including Medicaid or Medicare;
- impose restrictions or affirmative obligations on our or our CMO's operations, including costly new manufacturing requirements;
- close the facilities of a CMO; or
- seize or detain products or require a product recall.

If any of our product candidates for which we receive regulatory approval fails to achieve significant market acceptance among the medical community, patients or third-party payors, the revenue we generate from its sales will be limited and our business may not be profitable.

Our success will depend in substantial part on the extent to which our product candidates, if approved, are accepted by the medical community and patients and reimbursed by third-party payors, including government payors. The degree of market acceptance with respect to each of our approved products, if any, will depend upon a number of factors, including:

- the safety and efficacy of our product demonstrated in clinical studies;
- acceptance in the medical and patient communities of our product as a safe and effective treatment;
- the perceived advantages of our product over alternative treatments, including with respect to the incidence and severity of any adverse side effects and the cost of treatment;
- the indications for which our product is approved;
 - claims or other information (including limitations or warnings) in our product's approved labeling;
 - reimbursement and coverage policies of government and other third-party payors;
- pricing and cost-effectiveness of our product relative to alternative treatments;
- availability of alternative treatments;
- the prevalence of off-label substitution of chemically equivalent products or alternative treatments; and
- the resources we devote to marketing our product and restrictions on promotional claims we can make with respect to the product.

We cannot predict with reasonable accuracy whether physicians, patients, healthcare insurers or health maintenance organizations, or the medical community in general, will accept or utilize any of our products. If our product candidates are approved but do not achieve an adequate level of acceptance by these parties, we may not generate sufficient revenue to become or remain profitable. In addition, our efforts to educate the medical community and third-party payors regarding benefits of our products may require significant resources and may never be successful.

If we determine that a product candidate may not achieve adequate market acceptance or that the potential market size does not justify additional expenditure on the program, we may reduce our expenditures on the development and/or the process of seeking regulatory approval of the product candidate while we evaluate whether and on what timeline to move the program forward.

Even if we receive regulatory approval to market one or more of our product candidates in the U.S., we may never receive approval or commercialize our products outside of the U.S., which would limit our ability to realize the full commercial potential of our product candidates.

In order to market any products outside of the U.S., we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. The time required to obtain approval in other countries might differ from that required to obtain FDA approval. The regulatory

approval process in other countries may include all of the risks

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detailed above regarding FDA approval in the U.S., as well as other risks. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. Failure to obtain regulatory approval in other countries or any delay or setback in obtaining such approval could have the same adverse effects detailed above regarding FDA approval in the U.S. As described above, such effects include the risks that our product candidates may not be approved for all indications requested, which could limit the uses of our product candidates and have an adverse effect on product sales, and that such approval may be subject to limitations on the indicated uses for which the product may be marketed or require costly, post-marketing follow-up studies.

Risks Related to Our Intellectual Property

Our success will depend in part on obtaining and maintaining effective patent and other intellectual property protection for our product candidates and proprietary technology.

Our success will depend in part on our ability to:

- obtain and maintain patent and other exclusivity with respect to our products and their use;
- prevent third parties from infringing upon our proprietary rights;
- maintain proprietary know-how and trade secrets;
- operate without infringing upon the patents and proprietary rights of others; and
- obtain appropriate licenses to patents or proprietary rights held by third parties if infringement would otherwise occur or if necessary to secure exclusive rights to them, both in the U.S. and in foreign countries.

The patent and intellectual property positions of biopharmaceutical companies generally are highly uncertain, involve complex legal and factual questions, and have been and continue to be the subject of much litigation. There is no guarantee that we have or will develop or obtain the rights to products or processes that are patentable, that patents will issue from any pending applications or that claims allowed will be sufficient to protect the technology we develop or have developed or that is used by us, our CMOs or our other service providers. In addition, any patents that are issued to us may be limited in scope or challenged, invalidated, infringed or circumvented, including by our competitors, and rights we have under issued patents may not provide competitive advantages to us. If competitors can develop and commercialize technology and products similar to ours, our ability to successfully commercialize our technology and products may be impaired.

Patent applications in the U.S. are confidential for a period of time until they are published, and publication of discoveries in scientific or patent literature typically lags actual discoveries by several months. As a result, we cannot be certain that the inventors listed in any patent or patent application owned by us were the first to conceive of the inventions covered by such patents and patent applications (for U.S. patent applications filed before March 16, 2013), or that such inventors were the first to file patent applications for such inventions outside the United States and, after March 15, 2013, in the United States. In addition, changes in or different interpretations of patent laws in the United States and foreign countries may affect our patent rights and limit the number of patents we can obtain, which could permit others to use our discoveries or to develop and commercialize our technology and products without any compensation to us.

We also rely on unpatented know-how and trade secrets and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, through confidentiality agreements with employees, consultants, collaborators and others. We also have invention or patent assignment agreements with our employees and certain consultants. The steps we have taken to protect our proprietary rights, however, may not be adequate to preclude misappropriation of or otherwise protect our proprietary information or prevent infringement of our intellectual property rights, and we may not have adequate remedies for any such misappropriation or infringement. In addition, it is possible that inventions relevant to our business could be developed by a person not

bound by an invention assignment agreement with us or independently discovered by a competitor.

We also intend to rely on regulatory exclusivity for protection of our product candidates, if approved for commercial sale. Implementation and enforcement of regulatory exclusivity, which may consist of regulatory data protection and market protection, varies widely from country to country. Failure to qualify for regulatory exclusivity, or failure to obtain or maintain the extent or duration of such protections that we expect for our product candidates, if approved, could affect our decision on whether to market the products in a particular country or countries or could otherwise have an adverse impact on our revenue or our results of operations. For AIR001, which is administered via nebulization, we may rely on regulatory exclusivity for the combination of AIR001 and its delivery system. Other medications that alter pulmonary pressures include the delivery device in their U.S. and European market

labels, and are approved for use only with the specified proprietary delivery device. However, there is no assurance that our AIR001 product and its delivery system, if approved, will benefit from this type of market protection.

We may rely on trademarks, trade names and brand names to distinguish our products, if approved for commercial sale, from the products of our competitors. However, our trademark applications may not be approved. Third parties may also oppose our trademark applications or otherwise challenge our use of the trademarks in which case we may expend substantial resources to defend our trademarks and may enter into agreements with third parties that may limit our use of our trademarks. In the event that our trademarks are successfully challenged, we could be forced to rebrand our product, which could result in loss of brand recognition and could require us to devote significant resources to advertising and marketing these new brands. Further, our competitors may infringe our trademarks or we may not have adequate resources to enforce our trademarks.

Our success depends in large part on our ability to prevent competitors from duplicating or developing and commercializing equivalent versions of our product candidates, but patent protection may be difficult to obtain and any issued claims may be limited.

The potential use and therapeutic benefits of inorganic nitrite, such as sodium nitrite (the API in AIR001) have been known for decades. There is substantial prior art describing the uses of inorganic nitrite in a wide range of diseases and conditions. As a result, our ability to find novel and non-obvious uses of AIR001 is uncertain. Further, a patent examiner may combine numerous, disparate references in order to reject a claimed composition, formulation and/or use for obviousness. If the prior art suggests, even implicitly, the desirability of combining previously known elements, such as the use of AIR001 in a particular indication, the subsequent use of AIR001 in that indication may be unpatentable.

We have filed for patent protection in the U.S. and other countries to cover various methods of therapeutic use of our product candidates, including the use of inhaled inorganic nitrite for treating HFpEF. However, our pending patent applications may not issue as patents, and any issued patents may not provide us with significant competitive advantages, because the validity or enforceability of any of those patents may be challenged and, if instituted, one or more of the challenges may be successful. Patents may be challenged in the U.S. under post-grant review proceedings, inter partes reexamination, ex parte re-examination, or challenges in district court. Any patents issued in foreign jurisdictions may be subjected to comparable proceedings lodged in various foreign patent offices. These proceedings could result in either loss of the patent or loss or reduction in the scope of one or more of the claims of the patent. Even if a patent issues, and is held valid and enforceable, competitors may be able to design around our patents, such as by using pre-existing or newly developed technology, in which case competitors may not infringe our issued claims and may be able to market and sell products that compete directly with ours before our patents expire. In addition, our pending patent applications to cover use of AIR001 for treating HFpEF are jointly owned with an independent research and educational institution and until and unless we obtain an exclusive license to that co-owner's rights, it may license its rights to another third-party, which could negatively affect the value of our product candidate.

The patent prosecution process is expensive and time-consuming. We and any future licensors and licensees may not apply for or prosecute patents on certain aspects of our product candidates at a reasonable cost, in a timely fashion, or at all. We may not have the right to control the preparation, filing and prosecution of some patent applications related to our product candidates or technologies. As a result, these patents and patent applications may not be prosecuted and enforced in a manner consistent with the best interests of our company. It is also possible that we or any future licensors or licensees will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Further, it is possible that defects of form in the preparation or filing of our patent applications may exist, or may arise in the future, such as with respect to proper priority claims, inventorship, assignment, or claim scope. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid or unenforceable. In

addition, one or more parties may independently develop similar technologies or methods, duplicate our technologies or methods, or design around the patented aspects of our products, technologies or methods. Any of these circumstances could impair our ability to protect our products, if approved, in ways which may have an adverse impact on our business, financial condition and operating results.

Furthermore, the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in and outside of the United States. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical products or technology, or limit the duration of the patent protection of our technology and drugs. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing drugs similar or identical to ours.

Enforcement of intellectual property rights in countries outside the U.S., including China in particular, has been limited or non-existent. Future enforcement of patents and proprietary rights in many other countries will likely be problematic or unpredictable.

Moreover, the issuance of a patent in one country does not assure the issuance of a similar patent in another country. Claim interpretation and infringement laws vary by nation, so the extent of any patent protection is uncertain and may vary in different jurisdictions.

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.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and applications are required to be paid to the U.S. Patent and Trademark Office, or USPTO, and various governmental patent agencies outside of the U.S. in several stages over the lifetime of the patents and applications. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and after a patent has issued. There are situations in which non-compliance can result in decreased patent term adjustment or in abandonment or lapse of the patent or patent application, leading to partial or complete loss of patent rights in the relevant jurisdiction.

Third parties may claim that our products, if approved, infringe on their proprietary rights and may challenge the approved use or uses of a product or our patents rights through litigation or administrative proceedings, and defending such actions may be costly and time consuming, divert management attention away from our business, and result in an unfavorable outcome that could have an adverse effect on our business.

Our commercial success depends on our ability and the ability of our CMOs and component suppliers to develop, manufacture, market and sell our products and product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are or may be developing products. As the industries in which we operate (biopharmaceutical, specialty pharmaceutical, biotechnology and pharmaceutical) expand and more patents are issued, the risk increases that we will be subject to claims that our products or product candidates, or their use or manufacture, infringe the rights of others. Because patent applications can take many years to publish and issue, there currently may be pending applications, unknown to us, that may later result in issued patents that our products, product candidates or technologies infringe, or that the process of manufacturing our products or any of their respective component materials, or the component materials themselves, infringe, or that the use of our products, product candidates or technologies infringe.

We or our CMOs or component material suppliers may be exposed to, or threatened with, litigation by third parties alleging that our products, product candidates and/or technologies infringe their patents and/or other intellectual property rights, or that one or more of the processes for manufacturing our products or any of their respective component materials, or the component materials themselves, or the use of our products, product candidates or technologies, infringe their patents and/or other intellectual property rights. If a third-party patent or other intellectual property right is found to cover our products, product candidates, technologies or their uses, or any of the underlying manufacturing processes or components, we could be required to pay damages and could be unable to commercialize our products or use our technologies or methods unless we are able to obtain a license to the patent or intellectual property right. A license may not be available to us in a timely manner or on acceptable terms, or at all. In addition, during litigation, the third-party alleging infringement could obtain a preliminary injunction or other equitable remedy that could prohibit us from making, using, selling or importing our products, technologies or methods.

There generally is a substantial amount of litigation involving patent and other intellectual property rights in the industries in which we operate and the cost of such litigation may be considerable. We can provide no assurance that our product candidates or technologies will not infringe patents or rights owned by others, licenses to which might not be available to us in a timely manner or on acceptable terms, or at all. If a third party claims that we or our CMOs or

component material suppliers infringe its intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement and other intellectual property claims which, with or without merit, may be expensive and time consuming to litigate and may divert our management's time and attention from our core business;
- substantial damages for infringement, including the potential for treble damages and attorneys' fees, which we may have to pay if it is determined that the product and/or its use at issue infringes or violates the third party's rights;
- a court prohibiting us from selling or licensing the product unless the third-party licenses its intellectual property rights to us, which it may not be required to do;

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if a license is available from the third party, we may have to pay substantial royalties, fees and/or grant cross-licenses to the third party; and
redesigning our products or processes so they do not infringe, which may not be possible or may require substantial expense and time.

No assurance can be given that patents do not exist, have not been filed, or could not be filed or issued, which contain claims covering our products, product candidates or technology or those of our CMOs or component material suppliers or the use of our products, product candidates or technologies. Because of the large number of patents issued and patent applications filed in the industries in which we operate, there is a risk that third parties may allege they have patent rights encompassing our products, product candidates or technologies, or those of our CMOs or component material suppliers, or uses of our products, product candidates or technologies. With regard to AIR001, we are aware of issued patents and pending patent applications with claims related to compositions of sodium nitrite and therapeutic uses of sodium nitrite and/or inorganic nitrite. We do not believe that use of inhaled AIR001 to treat HFpEF, if approved, would infringe on issued patents. However, if AIR001 is approved for commercial sale, the third-party owners of patents issued currently or in the future may allege that our product infringes on their patents, in which case we may become involved in costly and time consuming litigation and/or administrative proceedings to defend the manufacture and/or use of our product, or we may agree to pay substantial amounts to obtain licenses from such parties, which could negatively affect our business prospects, operating results and financial condition.

In the future, it may be necessary for us to enforce our proprietary rights, or to determine the scope, validity and unenforceability of other parties' proprietary rights, through litigation or other dispute proceedings, which may be costly, and to the extent we are unsuccessful, adversely affect our rights. In these proceedings, a court or administrative body could determine that our claims, including those related to enforcing patent rights, are not valid or that an alleged infringer has not infringed our rights. The uncertainty resulting from the mere institution and continuation of any patent- or other proprietary rights-related litigation or interference proceeding could have a material and adverse effect on our business prospects, operating results and financial condition.

RISKS RELATED TO OUR INDUSTRY

We expect intense competition in the marketplace for our product candidates, should any of them receive regulatory approval.

The industries in which we operate (biopharmaceutical, specialty pharmaceutical, biotechnology and pharmaceutical) are highly competitive and subject to rapid and significant change. We are aware of many other organizations developing drug products and other therapies intended to treat or cure the diseases or conditions in which we are developing or plan to develop our product candidates. Developments by others may render potential application of any of our product candidates in a particular indication obsolete or noncompetitive, even prior to completion of its development and approval for that indication. If successfully developed and approved, we expect our product candidates will face intense competition. We may not be able to compete successfully against organizations with competitive products, particularly large pharmaceutical companies. Many of our potential competitors have significantly greater financial, technical and human resources than we do, and may be better equipped to develop, manufacture, market and distribute products. Many of these companies operate large, well-funded research, development and commercialization programs, have extensive experience in nonclinical and clinical studies, obtaining FDA and other regulatory approvals and manufacturing and marketing products, and have multiple products that have been approved or are in late-stage development. Smaller companies may also prove to be significant competitors, particularly through collaborative arrangements with large pharmaceutical and biotechnology companies. Furthermore, heightened awareness on the part of academic institutions, government agencies and other public and private research organizations of the potential commercial value of their inventions have led them to actively seek to commercialize the technologies they develop, which increases competition for investment in our programs. Competitive products may be more effective, or more effectively marketed and sold, than ours, which would have a

material adverse effect on our ability to generate revenue.

We are subject to uncertainty relating to healthcare reform measures and reimbursement policies that, if not favorable to our products, could hinder or prevent our products' commercial success, if any of our product candidates are approved.

The unavailability or inadequacy of third-party payor coverage and reimbursement could negatively affect the market acceptance of our product candidates and the future revenues we may expect to receive from those products. The commercial success of our product candidates, if approved, will depend in part on the extent to which the costs of such products will be covered by third-party payors, such as government health programs, commercial insurance and other organizations. These third-party payors are increasingly challenging the prices and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. If these third-party payors do not consider our products to be cost-effective compared to other therapies, they may not cover our products after approval as a benefit under their plans or, even if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis. In the case of products administered in an inpatient hospital setting, a level of payment that is inadequate to cover the cost to hospitals of providing and administering our products to patients, could delay market acceptance of or limit our ability to penetrate the markets for our products.

Significant uncertainty exists as to the reimbursement status for newly approved drug products, including coding, coverage and payment. There is no uniform policy requirement for coverage and reimbursement for drug products among third-party payors in the United States, therefore coverage and reimbursement for drug products can differ significantly from payor to payor. The coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate payment will be applied consistently or obtained. The process for determining whether a payor will cover and how much it will reimburse a product may be separate from the process of seeking approval of the product or for setting the price of the product. Even if reimbursement is provided, market acceptance of our products may be adversely affected if the amount of payment for our products proves to be unprofitable for healthcare providers or less profitable than alternative treatments or if administrative burdens make our products less desirable to use. Third-party payor reimbursement to providers of our products, if approved, may be subject to a bundled payment that also includes the procedure of administering our products. To the extent there is no separate payment for our product(s), there may be further uncertainty as to the adequacy of reimbursement amounts.

The continuing efforts of the government, private insurance companies, and other organizations to contain or reduce costs of healthcare may adversely affect:

- our ability to set an appropriate price for our products;
- the rate and scope of adoption of our products by healthcare providers;
- our ability to generate revenue or achieve or maintain profitability;
 - the future revenue and profitability of our potential customers, suppliers and collaborators; and
- our access to additional capital.

Our ability to successfully commercialize our products will depend in part on the extent to which governmental authorities, private health insurers and other organizations establish what we believe are appropriate coverage and reimbursement for our products. The containment of healthcare costs has become a priority of federal and state governments and the prices of drug products have been a focus in this effort. For example, there have been several recent U.S. Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. We expect that federal, state and local governments in the U.S. will continue to consider legislation directed at lowering the total cost of healthcare. In addition, in certain foreign markets, the pricing of drug products is subject to government control and reimbursement may in some cases be unavailable or insufficient. It is uncertain whether and how future legislation, whether domestic or abroad, could affect prospects for our product candidates or what actions federal, state, or private payors for healthcare treatment and services may take in response to any such healthcare reform proposals or legislation. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures reforms may prevent or limit our ability to generate revenue, attain profitability or commercialize our product candidates.

We face potential product liability exposure and, if successful claims are brought against us, we may incur substantial liability for a product or product candidate and may have to limit its commercialization. In the future, we anticipate that we will need to obtain additional or increased product liability insurance coverage and it is uncertain whether such increased or additional insurance coverage can be obtained on commercially reasonable terms, if at all.

Our business (in particular, the use of our product candidates in clinical studies and the sale of any products for which we obtain marketing approval) will expose us to product liability risks. Product liability claims might be brought against us by patients, healthcare providers, pharmaceutical companies or others selling our products. If we cannot successfully defend ourselves against any such claims, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for our products and loss of revenue;
- impairment of our business reputation;
- delays in enrolling patients to participate in our clinical studies;
- withdrawal of clinical study participants;
- a “clinical hold,” suspension or termination of a clinical study or amendments to a study design;

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- significant costs of related litigation;
- substantial monetary awards to patients or other claimants; and
- the inability to commercialize our products and product candidates.

We maintain limited product liability insurance for our clinical studies, but our insurance coverage may not reimburse us or may not be sufficient to reimburse us for all expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and, 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.

We expect that we will expand our insurance coverage to include the sale of commercial products if we obtain marketing approval of any of our product candidates, but we may be unable to obtain product liability insurance on commercially acceptable terms or may not be able to maintain such insurance at a reasonable cost or in sufficient amounts to protect us against potential losses. Large judgments have been awarded in class action lawsuits based on drug products that had unanticipated side effects. A successful product liability claim or series of claims brought against us could cause our stock price to fall and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

RISKS RELATED TO OUR COMMON STOCK

If we are unable to maintain compliance with NYSE MKT continued listing standards and policies, the NYSE MKT may commence proceedings to delist our common stock, and in some cases, determine to suspend trading in our common stock immediately without an opportunity to propose a plan that could enable us to regain compliance, which would likely cause the liquidity and market price of our common stock to decline and you could lose your investment.

Our common stock is listed on the NYSE MKT (“NYSE MKT” or the “Exchange”). The NYSE MKT retains substantial discretion to, at any time and without notice, suspend dealings in or remove from any security from listing. The NYSE MKT has adopted continued listing standards related to an issuer’s financial condition, operating results, disposal of assets, reduction in operations, compliance with listing agreements and SEC requirements, and the extent of public distribution and market value of the issuer’s listed security, and the Exchange will consider suspending dealings in, or delisting, securities of an issuer that does not meet those standards. For example, the NYSE MKT will consider suspending dealings in, or delisting, securities of an issuer that has stockholders’ equity of less than \$6 million if that issuer has sustained losses from continuing operations and/or net losses in its five most recent fiscal years. We have had a loss from operations and net loss in each of our five most recent fiscal years. As of December 31, 2016, our stockholders’ equity was \$9.8 million. If our stockholders’ equity falls below \$6 million, the Exchange may determine that we are no longer suitable for listing and may commence delisting proceedings pursuant Section 1003(a)(iii) of the NYSE MKT Company Guide.

The NYSE MKT will also normally consider suspending dealings in, or removing from the list, a common stock selling for a substantial period of time at a low price per share if the issuer fails to effect a reverse split of the stock within a reasonable time after being notified that the Exchange deems such action to be appropriate under the circumstances. We understand NYSE MKT policy to be that, if the 30-day average closing price of an issuer’s common stock is less than \$0.20 per share, the Exchange will alert the issuer to the fact that it may have a low selling price deficiency if, in six months, the 30-day average closing price of the issuer’s common stock is still, or again, less than \$0.20 per share. If, in six months, the 30-day average closing price of the issuer’s common stock is in fact less than \$0.20 per share, the issuer should expect to receive a deficiency letter from the Exchange notifying the issuer that it is below the continued listing criteria set forth in Section 1003(f)(v) of the NYSE MKT Company Guide and the issuer would have to submit a plan to the Exchange to regain compliance with its listing standards, have that plan accepted by the Exchange, and subsequently perform against that plan, otherwise the Exchange would commence delisting proceedings. The market price for our common stock historically has been highly volatile, and we expect it will continue to be highly volatile in the foreseeable future. If the 30-day average closing price of our common stock

falls below \$0.20 per share, we may, in six months from that time, be considered by the Exchange to be out of compliance with Section 1003(f)(v) of the NYSE MKT Company Guide and the Exchange may require us to effect a reverse split of our common stock within a reasonable time to regain compliance or otherwise commence delisting proceedings.

In addition, we are aware of a NYSE MKT policy that, if an issuer's common stock trades below \$0.06 per share, the staff of the Exchange will determine that issuer's stock is no longer suitable for listing on the NYSE MKT and will halt trading in and commence proceedings to delist that stock from the Exchange immediately. The issuer may appeal the delisting, but the issuer's stock will continue to be suspended from trading on the Exchange during the appeal process and the appeal may be unsuccessful.

There is no assurance that we will be able to maintain compliance with NYSE MKT continued listing standards and/or policies. The delisting of our common stock from the NYSE MKT likely would reduce the trading volume and liquidity in our

common stock, may lead to decreases in the trading price of our common stock, and may also materially impair our stockholders' ability to buy and sell shares. In addition, the delisting of our common stock could significantly impair our ability to raise additional capital, which may be necessary for to execute on our business strategy.

If our common stock were delisted and determined to be a "penny stock," a broker-dealer may find it more difficult to trade our common stock and an investor may find it more difficult to acquire or dispose of our common stock in the secondary market.

If our common stock was removed from listing with the NYSE MKT, it may be subject to the so-called "penny stock" rules. The SEC has adopted regulations that define a "penny stock" to be any equity security that has a market price per share of less than \$5.00, subject to certain exceptions, such as any securities listed on a national securities exchange. For any transaction involving a "penny stock," unless exempt, the rules impose additional sales practice requirements on broker-dealers, subject to certain exceptions. If our common stock were delisted and determined to be a "penny stock," a broker-dealer may find it more difficult to trade our common stock and an investor may find it more difficult to acquire or dispose of our common stock on the secondary market.

The market price of our common stock historically has been and likely will continue to be highly volatile.

The market price for our common stock historically has been highly volatile, and the market for our common stock has from time to time experienced significant price and volume fluctuations, based both on our operating performance and for reasons that appear to us unrelated to our operating performance. For instance, based on closing prices, the market price for our common stock dropped approximately 45% following our announcement of an underwritten public offering of equity securities on February 9, 2016, and it dropped approximately 80% following our announcement of top-line results of our Phase 3 clinical study of vepoloxamer in sickle cell disease on September 20, 2016. Conversely, the market price for our common stock increased by more than 55% during one trading day in January 2014, in the absence of any news release by us or rumors of which we were aware. The market price of our common stock may fluctuate significantly in response to a number of factors, including:

- the level of our financial resources;
- announcements of entry into or consummation of a financing or strategic transaction;
- results from a clinical study of a product candidate;
- delays in the completion of our clinical studies or termination of a clinical study, including due to difficulties with patient enrollment or safety issues or inability to produce sufficient quantities of clinical trial material;
- FDA or international regulatory actions and regulatory developments in the U.S. and foreign countries;
- announcements of new products or technologies, commercial relationships or other events (including clinical study results and regulatory events and actions) by us or our competitors;
- announcements of difficulties or delays in commercial manufacture or supply of our drug products;
- market conditions in the pharmaceutical, biopharmaceutical, specialty pharmaceutical and biotechnology sectors;
- developments concerning intellectual property rights generally or those of us or our competitors;
- changes in securities analysts' estimates of our financial performance or deviations in our business and the trading price of our common stock from the estimates of securities analysts;
- events affecting any future collaborations, commercial agreements and grants;
- fluctuations in stock market prices and trading volumes of similar companies;
- sales of large blocks of our common stock, including sales by significant stockholders, our executive officers or our directors or pursuant to shelf or resale registration statements that register shares of our common stock that may be sold by us or certain of our current or future stockholders;
 - discussion of us or our stock price by the financial and scientific press and in online investor communities;
- commencement of delisting proceedings by the NYSE MKT;

- additions or departures of key personnel; and
- changes in third-party payor coverage or reimbursement policies.

As evidenced by the September 2016 decline, the realization of any of the foregoing could have a dramatic and adverse impact on the market price of our common stock. In addition, class action litigation has often been instituted against companies whose securities have experienced a substantial decline in market price. Moreover, regulatory entities often undertake investigations of investor transactions in securities that experience volatility following an announcement of a significant event or condition. Any such litigation brought against us or any such investigation involving our investors could result in substantial costs and a diversion of management's attention and resources, which could harm our business, operating results and financial condition.

Our stock price could decline significantly based on progress with and results of our clinical studies and regulatory agency decisions affecting development of our product candidates.

We expect announcements of progress with and results of clinical studies of our product candidates and regulatory decisions (by us, the FDA, or another regulatory agency) to affect our stock price. Stock prices of companies in our industry have declined significantly when such results and decisions were unfavorable or perceived to be negative or discouraging or when a product candidate did not otherwise meet expectations, and, as discussed above, the price of our common stock dropped significantly following our September 20, 2016 announcement that our Phase 3 clinical study of vepoloxamer in sickle cell disease did not meet the primary efficacy endpoint. If progress in clinical studies or study results are not viewed favorably by us or third parties, including investors, analysts, potential collaborators, the academic and medical communities and regulators, our stock price could decline significantly and you could lose your investment in our common stock.

We may report top-line or interim clinical and nonclinical study data from time to time, which is based on preliminary analysis of then-available data. Such preliminary findings and conclusions are subject to change following a more comprehensive review of the study data and, in the case of interim data, completion of the study. In addition, results of clinical and nonclinical studies often are subject to different interpretations. We may interpret or weigh the importance of study data differently than third parties, including those noted above. Others may not accept or agree with our analysis of study data, which could impact the approvability of our product candidates and/or the value of our development programs and our company in general.

Sales of substantial amounts of our common stock or the perception that such sales may occur could cause the market price of our common stock to decline significantly, even if our business is performing well.

The market price of our common stock could decline as a result of sales by, or the perceived possibility of sales by, us or our existing stockholders of shares of our common stock. Sales by our existing stockholders might also make it more difficult for us to sell equity securities at a time and price that we deem appropriate. Under our existing ATM program, as of December 31, 2016, we may sell up to approximately \$18.0 million of additional shares of our common stock. The shelf registration statement on Form S-3 under which the ATM program is registered may be used to register the sale and issuance of more than \$99 million of additional securities, subject to limitations if our public float is less than \$75 million. In addition, as of March 2, 2017, we have outstanding warrants to purchase approximately 81 million additional shares of our common stock. All of those warrants have an exercise price of less than \$1.00 per share; however, based on the closing price of our common stock on March 2, 2017, no outstanding warrants are in-the-money. Collectively, the ATM program, the shelf registration statement and any in-the-money warrants, may increase the likelihood of sales of substantial amounts of our shares, or the perception that substantial sales may occur, by us or our existing securityholders from time to time, which could cause the market price of our common stock to decline significantly.

Anti-takeover provisions in our charter documents and under Delaware law may make an acquisition of us, which may be beneficial to our stockholders, more difficult, which could depress our stock price.

We are incorporated in Delaware. Certain anti-takeover provisions of Delaware law and our charter documents as currently in effect may make a change in control of our company more difficult, even if a change in control would be beneficial to our stockholders. Our bylaws limit who may call a special meeting of stockholders and establish advance notice requirements for nomination of individuals for election to our board of directors or for proposing matters that can be acted upon at stockholders' meetings. Delaware law also prohibits corporations from engaging in a business combination with any holders of 15% or more of their capital stock until the holder has held the stock for three years unless, among other possibilities, the board of directors approves the transaction. Our board of directors may use these provisions to prevent changes in the management and control of our company. Also, under applicable Delaware law, our board of directors may adopt additional anti-takeover measures in the future. In addition, provisions of certain compensatory contracts with our management, such as equity award agreements, may have an anti-takeover effect by resulting in accelerated vesting of outstanding equity securities held by our executive officers.

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Because we do not expect to pay dividends with respect to our common stock in the foreseeable future, you must rely on stock appreciation for any return on your investment.

We have paid no cash dividends on any of our common stock to date, and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. As a result, with respect to our common stock, we do not expect to pay any cash dividends in the foreseeable future, and payment of cash dividends, if any, will also depend on our financial condition, results of operations, capital requirements and other factors and will be at the discretion of our board of directors. Furthermore, we are subject to various laws and regulations that may restrict our ability to pay dividends and we may in the future become subject to contractual restrictions on, or prohibitions against, the payment of dividends. Currently, our debt facility with Hercules prohibits us from declaring and paying any cash dividend on any class of stock or other equity interest. Due to our intent to retain any future earnings rather than pay cash dividends on our common stock and applicable laws, regulations and contractual obligations that may restrict our ability to pay dividends on our common stock, the success of your investment in our common stock will likely depend entirely upon any future appreciation and our common stock may not appreciate.

If we were to issue shares of our common stock or preferred stock that are available for issuance, our stock price could decline.

We have 500,000,000 shares of authorized common stock and, as of March 2, 2017, approximately 115 million of such authorized shares were not outstanding or reserved for issuance under outstanding warrants, options, equity incentive plans or other rights. Subject to applicable securities laws and stock exchange listing requirements, our board of directors is authorized under our charter documents to sell and issue our authorized, but unissued, common stock without stockholder approval and may do so to satisfy our capital requirements or finance the expansion of our product pipeline. Our board of directors also is authorized to issue and sell up to 1,000,000 shares of preferred stock without stockholder approval, at a purchase price approved by the board. The preferred stock may have rights that are superior to the rights of the holders of our common stock. The sale or the proposed sale of substantial amounts of our common stock, preferred stock and/or securities convertible into shares of our common or preferred stock in the public markets may adversely affect the market price of our common stock. Our stockholders may also experience substantial dilution.

Item 1B. Unresolved Staff Comments.

We do not have any unresolved comments issued by the SEC staff.

Item 2. Properties.

We sublease approximately 13,700 square feet of office space for our headquarters in San Diego, California. Approximately three years remain on the sublease term. If the proposed merger with Savara is consummated, we do not anticipate an ongoing need for these facilities. As such, we are seeking to sublease these facilities for the remaining sublease term. We have no laboratory, research or manufacturing facilities.

Item 3. Legal Proceedings.

From time to time, we may become involved in various claims and legal proceedings. Regardless of outcome, litigation and other legal proceedings can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors. We are not currently a party to any material pending litigation or other material legal proceeding.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Our common stock trades under the symbol "MSTX" on the NYSE MKT equities market. The following table sets forth the high and low sale prices for our common stock in each full quarterly period within the two most recent fiscal years.

	Sales Price			
	2016		2015	
	High	Low	High	Low
First Quarter	\$0.50	\$0.21	\$0.63	\$0.42
Second Quarter	\$0.48	\$0.27	\$0.58	\$0.46
Third Quarter	\$0.71	\$0.09	\$0.60	\$0.38
Fourth Quarter	\$0.16	\$0.07	\$0.59	\$0.37

As of March 2, 2017, we had approximately 116 record holders of our common stock. The number of beneficial owners is substantially greater than the number of record holders because a large majority of our outstanding common stock is held of record through brokerage firms in "street name."

Dividend Policy

We have never declared or paid any cash dividends on our common stock and do not anticipate declaring or paying any cash dividends on our common stock in the foreseeable future. We expect to retain all available funds and any future earnings to support operations and fund the development and growth of our business. Our board of directors will determine whether we pay and the amount of future dividends (including cash dividends), if any.

In connection with previous preferred stock financings, we have agreed to charter restrictions on our ability to pay cash dividends or distributions on our common stock for so long as any shares of such preferred stock are outstanding, unless we obtain prior written consent from the holders of such preferred stock. Although currently there are no such restrictions on our ability to pay dividends on our common stock, we may agree to similar restrictions in the future.

Performance Graph

The following graph shows a comparison of the total cumulative returns of an investment of \$100 in cash from December 31, 2011 through December 31, 2016 in (i) our common stock, (ii) the NASDAQ Composite Index and (iii) the NASDAQ Biotechnology Index. The comparisons in the graph are required by the SEC and are not intended to forecast or be indicative of the possible future performance of our common stock.

Recent Sales of Unregistered Securities

The information required regarding sales of unregistered securities during the year ended December 31, 2016 previously has been provided in a Quarterly Report on Form 10-Q or a Current Report on Form 8-K.

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Item 6. Selected Financial Data.

The following data have been derived from our audited consolidated financial statements, including the consolidated balance sheets at December 31, 2016 and 2015 and the related consolidated statements of operations for each of the three years ended December 31, 2016, 2015 and 2014, and related notes appearing elsewhere in this report. The consolidated statements of operations data for the years ended December 31, 2013 and 2012 and the balance sheet data as of December 31, 2014, 2013 and 2012 are derived from our audited consolidated financial statements that are not included in this report. You should read the selected financial data set forth below in conjunction with “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our consolidated financial statements and related notes appearing elsewhere in this report.

	Years ended December 31,				
	2016	2015	2014	2013	2012
	(in thousands, except per share amounts)				
Consolidated Statement of Operations Data:					
Revenues	\$128	\$—	\$—	\$—	\$—
Operating expenses:					
Research and development	20,793	28,264	19,435	12,902	8,088
Selling, general and administrative	9,342	10,963	9,488	8,518	7,519
Transaction-related expenses	301	—	271	80	(69)
Impairment of IPR&D	6,049	—	—	—	—
Depreciation and amortization	99	146	85	39	90
Total operating expenses	36,584	39,373	29,279	21,539	15,628
Loss from operations	(36,456)	(39,373)	(29,279)	(21,539)	(15,628)
Interest income	122	130	69	60	74
Interest expense	(2,132)	(603)	—	—	—
Other income/(expense), net	(43)	4	508	(1)	(5)
Loss before income taxes	(38,509)	(39,842)	(28,702)	(21,480)	(15,559)
Income tax benefit	2,409	—	—	—	—
Net loss	\$(36,100)	\$(39,842)	\$(28,702)	\$(21,480)	\$(15,559)
Net loss per share - basic and diluted	\$(0.17)	\$(0.25)	\$(0.23)	\$(0.28)	\$(0.33)
Weighted average shares outstanding - basic					
and diluted	208,484,370	162,219,116	122,409,183	76,585,752	47,641,043
At December 31,					
	2016	2015	2014	2013	2012
	(in thousands)				
Consolidated Balance Sheet Data:					
Cash, cash equivalents and investment	11,282	40,981	57,289	44,392	36,511
securities					
Working capital	7,319	19,079	49,965	40,695	34,603
Total assets	17,922	54,217	70,500	55,250	46,972
Total stockholders' equity	9,759	23,889	58,658	47,808	41,792

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with the consolidated financial statements and related notes appearing elsewhere in this report. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties, and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors, including but not limited to those identified under Item 1A "Risk Factors" in this report.

Overview

We are a biopharmaceutical company developing clinical-stage therapies for serious or life-threatening diseases with significant unmet needs. Our lead product candidate, AIR001, a sodium nitrite solution for inhalation via nebulization, has demonstrated positive hemodynamic benefits in patients with heart failure with preserved ejection fraction, or HFpEF, and pulmonary hypertension, and currently is in clinical development for HFpEF. As discussed in Part I, Item 1, "Business" of this report, three investigator-sponsored Phase 2 studies of AIR001 in patients with HFpEF are being conducted by prestigious research institutions, including the 100-patient, randomized, double-blind, placebo-controlled crossover INDIE-HFpEF study being conducted by the Heart Failure Clinical Research Network, known as the HFN. Positive interim results from another of those ongoing studies were published in the Journal of Clinical Investigation in November 2016. Results from the INDIE-HFpEF study are expected in the first quarter of 2018.

Our second product candidate, vepoloxamer (also known as MST-188), is in preclinical development to evaluate its potential therapeutic use in ischemic stroke. Vepoloxamer was previously in Phase 3 and Phase 2 clinical development in sickle cell disease and heart failure, respectively, but, in September 2016, following negative top-line results of the Phase 3 study in sickle cell disease known as EPIC, we determined to discontinue clinical development of vepoloxamer and wind down all of the clinical studies. Our current development of vepoloxamer is limited to completing an NIH grant-funded nonclinical study of vepoloxamer in ischemic stroke. We do not plan to direct any additional capital toward the development of vepoloxamer during the next 12 months.

We have devoted substantially all of our resources to research and development, or R&D, and to acquisition of our product candidates. We have not yet marketed or sold any products or generated any significant revenue and we have incurred significant annual operating losses since inception. We incurred losses from operations of \$36.5 million, \$39.4 million and \$29.3 million for the years ended December 31, 2016, 2015 and 2014, respectively. As of December 31, 2016, we had an accumulated deficit of \$311.1 million. Our cash, cash equivalents, and investment securities were \$11.3 million and our working capital was \$7.3 million as of December 31, 2016.

Our planned operating activities call for expenditures over the next 12 months that exceed our working capital as of December 31, 2016 and our ability to raise additional capital as needed is uncertain. We are focused on managing our operating expenses and maintaining adequate capital to run our business through consummation of the proposed merger with Savara (discussed below). In addition to managing our operating expenses, we are exploring opportunities to monetize our vepoloxamer-related assets prior to consummation of the merger. Under the merger agreement, the exchange ratio is subject to adjustment based on our net cash balance at closing of the transaction (with "net cash" as specifically defined in the merger agreement) and our company's and Savara's capitalization at closing. To the extent our net cash at closing is less than zero dollars, the exchange ratio may be adjusted in a manner that would reduce the ownership percentage of our stockholders in the combined company. There can be no assurance that we will be successful in completing the merger with Savara, monetizing our vepoloxamer-related assets, or maintaining or raising sufficient additional capital to fund continued operations. We estimate that our existing capital resources will be sufficient to fund our operations into the second quarter of 2017. If we are unable to consummate the merger with Savara, significant additional funds would be needed to fund our operations to execute on our business strategy

and advance the AIR001 program and we may not be successful in those efforts. These circumstances raise substantial doubt about our ability to continue as a going concern. Our financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from the outcome of this uncertainty.

Proposed Merger with Savara and Change in Control

On January 6, 2017, we entered into an Agreement and Plan of Merger and Reorganization with Savara Inc., a privately-held, clinical-stage specialty pharmaceutical company focused on the development and commercialization of novel therapies for the treatment of serious or life-threatening rare respiratory diseases. Pursuant to the merger agreement, subject to the satisfaction or waiver of the conditions set forth in the agreement, including the approval of our stockholders and Savara's stockholders, our wholly-owned subsidiary, Victoria Merger Corp. (formed for the purpose of this transaction), will merge with and into Savara, with Savara surviving the merger as a wholly-owned subsidiary of our company and Savara stockholders receiving newly issued shares of our common stock in exchange for their Savara stock. The transactions contemplated by the merger agreement will result in a change in

control of our company, with approximately 76% of the shares of our common stock outstanding after consummation of the merger expected to be held by the former Savara securityholders and approximately 24% of such shares expected to be held by our stockholders, assuming no adjustments are required under the merger agreement as a result of our net cash at closing being less than zero dollars or changes to our company's or Savara's capitalization at closing of the transaction relative to when we entered into the merger agreement. The merger agreement contemplates that, immediately following the merger, the combined company's name will be changed from "Mast Therapeutics, Inc." to "Savara Inc.," the board of directors will consist of seven members, five of which will be the current directors of Savara and two of which will be independent directors designated by us, which are expected to be two of our current independent directors, and the executive officers of the combined company will be designated by Savara with Savara's Chief Executive Officer, Robert Neville, being the combined company's Chief Executive Officer, and Savara's Chief Financial Officer, David Lowrance, being the combined company's Chief Financial Officer. The transaction is expected to close in the second quarter of 2017.

The combined company's pipeline would include:

- AeroVanc, an inhaled dry-powder vancomycin to treat chronic methicillin-resistant *Staphylococcus aureus* (MRSA) pulmonary infection in cystic fibrosis (CF), which is in preparation for a pivotal Phase 3 clinical study;
- Molgradex, an inhaled nebulized GM-CSF to treat pulmonary alveolar proteinosis (PAP), which is currently in Phase 2/3 development; and
- AIR001, our lead product candidate.

See Part I, Item 1, "Business," in this report for additional information about the merger agreement and proposed merger with Savara.

Acquisition of Aires Pharmaceuticals

In February 2014, we acquired Aires Pharmaceuticals, Inc., a privately-held corporation, in a merger transaction, which resulted in Aires becoming our wholly-owned subsidiary. Upon completion of the merger, we issued an aggregate of 1,049,706 unregistered shares of our common stock to former Aires stockholders and, in September 2014, following a six-month "holdback" period, we issued an aggregate of 4,053,996 additional unregistered shares of our common stock to former Aires stockholders in accordance with the merger agreement. There are no milestone or earn-out payments under the merger agreement. Accordingly, the total merger consideration was 5,103,702 shares, which represented approximately 5% of our outstanding common stock as of the acquisition date.

Critical Accounting Policies and Significant Judgments and Estimates

Our discussion and analysis of our financial condition and results of operations included in this annual report is based upon consolidated financial statements that we have prepared in accordance with U.S. generally accepted accounting principles, or U.S. GAAP. The preparation of these financial statements requires us to make a number of estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses in these financial statements and accompanying notes. On an ongoing basis, we evaluate these estimates and assumptions, including those related to determination of the fair value of goodwill and acquired in-process research and development, or IPR&D, and recognition of R&D expenses and share-based compensation. We base our estimates on historical information, when available, and assumptions believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities not readily apparent from other sources. Actual results may differ materially from these estimates under different assumptions or conditions.

We believe the following accounting estimates are those that can have a material impact on our financial condition or operating performance and involve substantial subjectivity and judgment in the application of our accounting policies to account for highly uncertain matters or the susceptibility of such matters to change. The following is not intended to be a comprehensive discussion of all of our significant accounting policies. See the notes accompanying our financial statements appearing in this report for a summary of all of our significant accounting policies and other disclosures required by U.S. GAAP.

Accrued Research and Development Expenses. As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify 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. Many 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 as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time.

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We periodically confirm the accuracy of our estimates with the service providers and make adjustments, if necessary. The majority of our accrued expenses relate to R&D services and related expenses. Examples of estimated accrued R&D expenses include:

- fees paid to contract research organizations, or CROs, in connection with clinical studies;
- fees paid to investigative sites and investigators in connection with clinical studies;
- fees paid to contract manufacturing organizations, or CMOs, in connection with process development activities and production of nonclinical and clinical trial material;
- fees paid to vendors in connection with nonclinical development activities; and
- fees paid to consultants for regulatory-related advisory and data management services.

We base our accrued expenses related to CROs and CMOs on our estimates of the services received and efforts expended pursuant to purchase orders or contracts with multiple service providers that we engage to conduct and manage our clinical studies and manufacture our clinical trial material on our behalf. The financial terms of our arrangements with our CROs and CMOs are subject to negotiation, vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful completion of specified process development activities or the successful enrollment of patients and the completion of clinical study milestones. In accruing these service fees, we estimate, as applicable, the time period over which services will be performed (e.g., enrollment of patients, activation of clinical sites, etc.). If the actual timing varies from our estimate, we adjust the accrual accordingly. In addition, there may be instances in which payments made to service providers will exceed the level of services provided and result in a prepayment of R&D expense, which we report as an asset. The actual costs and timing of clinical studies and research-related manufacturing are uncertain and subject to change depending on a number of factors. Differences between actual costs of these services and the estimated costs that we have accrued in a prior period are recorded in the subsequent period in which the actual costs become known to us. Historically, these differences have not resulted in material adjustments, but such differences may occur in the future and have a material impact on our consolidated results of operations or financial position.

Business Combinations. We account for business combinations, such as our acquisitions of SynthRx in April 2011 and Aires Pharmaceuticals in February 2014, in accordance with Accounting Standards Codification, or ASC, Topic 805, Business Combinations, which requires the purchase price to be measured at fair value. When the purchase consideration consists entirely of shares of our common stock, we calculate the purchase price by determining the fair value, as of the acquisition date, of shares issued in connection with the closing of the acquisition and, if the transaction involves contingent consideration based on achievement of milestones or earn-out events, the probability-weighted fair value, as of the acquisition date, of shares issuable upon the occurrence of future events or conditions pursuant to the terms of the agreement governing the business combination. If the transaction involves such contingent consideration, our calculation of the purchase price involves probability inputs that are highly judgmental due to the inherent unpredictability of drug development, particularly by development-stage companies such as ours. We recognize estimated fair values of the tangible assets and intangible assets acquired, including IPR&D, and liabilities assumed as of the acquisition date, and we record as goodwill any amount of the fair value of the tangible and intangible assets acquired and liabilities assumed in excess of the purchase price.

Goodwill and Acquired IPR&D. In accordance with ASC Topic 350, Intangibles – Goodwill and Other, or ASC Topic 350, our goodwill and acquired IPR&D are determined to have indefinite lives and, therefore, are not amortized. Instead, they are tested for impairment annually and between annual tests if we become aware of an event or a change in circumstances that would indicate the carrying value may be impaired. We perform our annual impairment testing as of September 30 of each year, or, in the case of initially acquired IPR&D, on the first anniversary of the date we acquired it and subsequently on September 30. Pursuant to Accounting Standards Update, or ASU, No. 2011-08, Intangibles – Goodwill and Other (Topic 350): Testing Goodwill for Impairment, and No. 2012-02, Intangibles – Goodwill and Other (Topic 350): Testing Indefinite-Lived Intangible Assets for Impairment, we have the option to first assess qualitative factors to determine whether the existence of events or circumstances leads us to determine that

it is more likely than not (that is, a likelihood of more than 50%) that our goodwill or our acquired IPR&D is impaired. If we choose to first assess qualitative factors and we determine that it is not more likely than not goodwill or acquired IPR&D is impaired, we are not required to take further action to test for impairment. We also have the option to bypass the qualitative assessment and perform only the quantitative impairment test, which we may choose to do in some periods but not in others.

If we perform a quantitative assessment of goodwill, we utilize the two-step approach prescribed under ASC Topic 350. Step 1 requires a comparison of the carrying value of a reporting unit, including goodwill, to its estimated fair value. We test for impairment at the entity level because we operate on the basis of a single reporting unit. If our carrying value exceeds our fair value, we then perform Step 2 to measure the amount of impairment loss, if any. In Step 2, we estimate the fair value of our individual assets, including identifiable intangible assets, and liabilities to determine the implied fair value of goodwill. We then compare the carrying

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value of our goodwill to its implied fair value. The excess of the carrying value of goodwill over its implied fair value, if any, is recorded as an impairment charge.

Similarly, if we perform a quantitative assessment of IPR&D, we compare its carrying value to its estimated fair value to determine whether an impairment exists. In previous years, due to a lack of Level 1 or Level 2 inputs (as defined in Note 6, "Fair Value of Financial Instruments," of the Notes to Consolidated Financial Statements appearing in this report), the Multi-Period Excess Earnings Method, or MPEEM, which is a form of the income approach, was used to estimate the fair value of acquired IPR&D when performing a quantitative assessment. Under the MPEEM, the fair value of an intangible asset is equal to the present value of the asset's projected incremental after-tax cash flows (excess earnings) remaining after deducting the market rates of return on the estimated value of contributory assets (contributory charge) over its remaining useful life. The MPEEM uses primarily Level 3 inputs (as defined in Note 6, "Fair Value of Financial Instruments," of the Notes to Consolidated Financial Statements appearing in this report). In evaluating potential impairment of our vepoloxamer-related acquired IPR&D as of December 31, 2016, we utilized Level 2 inputs in the form of expressions of interest in the vepoloxamer-related assets received recent to the valuation date to estimate fair value. While we continue to evaluate opportunities to monetize our vepoloxamer assets, we can provide no assurances that we will be able to do so. However, we believe that an approach based on third party expressions of interest is a more appropriate method for assessing fair value in the context of our current situation. We have limited time to further develop strategic opportunities for our vepoloxamer assets before the proposed merger with Savara is completed, and, as Savara did not ascribe any significant value to the vepoloxamer assets in the negotiation of the merger agreement, we do not believe it is appropriate to consider long-term cash flows that may only be achieved with significant further clinical development.

Our determinations as to whether, and, if so, the extent to which, goodwill and acquired IPR&D become impaired are highly judgmental and, in the case of applying the MPEEM approach to estimate fair value, are based on significant assumptions regarding our projected future financial condition and operating results, changes in the manner of our use of the acquired assets, development of our acquired assets or our overall business strategy, and regulatory, market and economic environment and trends.

Share-based Compensation Expenses. We account for share-based compensation awards granted to employees, including non-employee members of our board of directors, in accordance with ASC Topic 718, Compensation – Stock Compensation. Compensation expense for all share-based awards is based on the estimated fair value of the award on its date of grant and recognized on a straight-line basis over its vesting period. As share-based compensation expense is based on awards ultimately expected to vest, it is reduced for estimated forfeitures. We estimate forfeitures at the time of grant based on the expected forfeiture rate for our unvested stock options, which is based in large part on our historical forfeiture rates, but also on assumptions believed to be reasonable under the circumstances. We revise our estimates in subsequent periods if actual forfeitures differ from those estimates. Although share-based compensation expense can be significant to our consolidated financial statements, it does not involve the payment of any cash by us.

We estimate the grant date fair value of a stock option award using the Black-Scholes option-pricing model, or Black-Scholes model. In determining the grant date fair value of a stock option award under the Black-Scholes model, we must make a number of assumptions, including the term of the award, the volatility of the price of our common stock over the term of the award, and the risk-free interest rate. Changes in these or other assumptions could have a material impact on the compensation expense we recognize.

Results of Operations – Overview

We operate our business and evaluate our company on the basis of a single reportable segment, which is the business of developing therapies for serious or life-threatening diseases.

Revenue

We have not generated any revenue from product sales to date, and we do not expect to generate revenue from product sales until such time, if any, that we have obtained approval from a regulatory agency to sell one or more of our product candidates, which we cannot predict with certainty will occur. If we enter into any licensing or other collaborative arrangements regarding our development programs, we may recognize revenue from those arrangements prior to commercial sale of any products.

We recognize revenues from federal government research grants during the period in which we receive the grant funds, or their collection is reasonably assured, and we incur the qualified expenditures. The expenditures are reflected as a component of R&D expense in the Statements of Operations and Comprehensive Loss.

Operating Expenses

Research and Development Expenses. We maintain and evaluate our R&D expenses by the type of cost incurred rather than by project. We do this primarily because we outsource a substantial portion of our work and our R&D personnel and consultants work across multiple programs rather than dedicating their time to one particular program. We categorize our R&D expenses as external

clinical study fees and expenses, external nonclinical study fees and expenses, personnel costs and share-based compensation expense. The major components of our external clinical study fees and expenses are fees and expenses related to CROs and clinical study investigative sites and investigators. The major components of our external nonclinical study fees and expenses are fees and expenses related to preclinical studies and other nonclinical testing, research-related manufacturing, and quality assurance and regulatory affairs services, and preparation of a NDA for vepoloxamer. Research-related manufacturing expenses include costs associated with producing and/or purchasing active pharmaceutical ingredient (API), conducting process development activities, producing clinical trial material, producing material for stability testing to support regulatory filings, related labeling, testing and release, packaging and storing services, related consulting fees and costs related to purchasing nebulizers for administration of AIR001. Impairment losses on R&D-related manufacturing equipment are also considered research-related manufacturing expenses. Personnel costs relate to employee salaries, benefits, severance (as applicable), and related costs.

A general understanding of drug development is critical to understanding our results of operations and, particularly, our R&D expenses. Drug development in the U.S. and most countries throughout the world is a process that includes several steps defined by the U.S. Food and Drug Administration, or FDA, and similar regulatory authorities in foreign countries. The FDA approval processes relating to new drug products differ depending on the nature of the particular product candidate for which approval is sought. With respect to any product candidate with active ingredients not previously approved by the FDA, a prospective drug product manufacturer is required to submit a new drug application, or NDA, that includes complete reports of pre-clinical, clinical and laboratory studies and extensive manufacturing information to demonstrate the product candidate's safety and effectiveness. Generally, an NDA must be supported by at least phase 1, 2 and 3 clinical studies, with each study typically more expensive and lengthy than the previous study.

Future expenditures on R&D programs are subject to many uncertainties, including the number of clinical studies required to be conducted for each development program and whether we will develop a product candidate with a partner or independently. At this time, due to such uncertainties and the risks inherent in drug product development and the associated regulatory process, we cannot estimate with any reasonable certainty the duration of or costs to complete our R&D programs, or whether or when or to what extent revenues will be generated from the commercialization and sale of any of our product candidates. The duration and costs of our R&D programs, in particular, the duration and costs associated with clinical studies and research-related manufacturing, can vary significantly as a result of a variety of factors, including:

- the number of clinical and nonclinical studies necessary to demonstrate the safety and efficacy of a product candidate in a particular indication;
- the number of patients who participate in each clinical study;
- the number and location of sites included and the rate of site approval in each clinical study;
- the rate of patient enrollment and ratio of randomized to evaluable patients in each clinical study;
- the duration of patient treatment and follow-up;
- the potential additional safety monitoring or other studies requested by regulatory agencies;
- the time and cost to manufacture clinical trial material and commercial product, including process development and scale-up activities, and to conduct stability studies, which can last several years;
- the availability and cost of comparative agents used in clinical studies;
- the timing and terms of any collaborative or other strategic arrangements that we may establish; and
- the cost, requirements, timing of and the ability to secure regulatory approvals.

We regularly evaluate the prospects of our R&D programs, including in response to available scientific, nonclinical and clinical data, our assessments of a product candidate's market potential and our available resources, and make determinations as to which programs to pursue and how much funding to direct to each one.

Selling, General and Administrative Expenses. Selling, general and administrative, or SG&A, expenses primarily consist of salaries, benefits, severance (as applicable), and related costs for personnel in executive, finance and accounting, legal and marketing functions, and professional and consulting fees for accounting, legal, investor relations, business development, commercial strategy and research, human resources and information technology services. Other SG&A expenses include facility lease and insurance costs and in-licensing costs for third-party intellectual property, if any.

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Transaction-Related Expenses. Transaction-related expenses consist of legal, accounting, financial and business development advisory fees associated with the evaluation of potential acquisition targets and execution of acquisition transactions, including our acquisition of Aires and potential merger with Savara.

Interest Income. Interest income includes interest earned on our cash, cash equivalent and investment security balances.

Interest Expense. Interest expense consists of interest payments made and interest expense related to debt issuance costs and debt discount under our debt facility with Hercules and interest expense associated with payments under capital leases of equipment.

Other (Expense)/Income, Net. Other (expense)/income, net includes the bargain purchase gain related to the acquisition of Aires in 2014, as well as unrealized and realized gains and losses from foreign currency transactions and other non-operating gains and losses.

Results of Operations – Comparison of 2016 and 2015

Revenue. We recognized \$128,000 of revenue for the year ended December 31, 2016. The revenue represents reimbursement of costs related to the nonclinical study of vepoloxamer that is being funded by a grant from the National Institute of Neurological Disorders and Stroke of the NIH. We recognized no revenue for the year ended December 31, 2015.

Operating Expenses. The following table illustrates the types of operating expenses we incurred in 2016 and 2015 and their respective percent of our total operating costs for those periods:

	Operating Expenses	
	Years Ended	
	December	
	31,	
	2016	2015
Research and development	57 %	72 %
Selling, general and administrative	26 %	28 %
Transaction-related expenses	1 %	—
Impairment of IPR&D	16 %	—
Depreciation and amortization	0 %	0 %
Total operating expenses	100 %	100 %

R&D Expenses. In 2016, our most significant R&D expenses were external costs associated with the EPIC study, research-related manufacturing for vepoloxamer, our Phase 2 study of vepoloxamer in heart failure and preparing an NDA for vepoloxamer. These expenses consisted primarily of CRO and CMO expenses, clinical study and regulatory-related consulting expenses, and study site expenses, which include start-up costs as well as patient costs. In 2015, our most significant R&D expenses were external costs associated with the EPIC study, our Phase 2 studies of vepoloxamer in acute limb ischemia, or ALI (which we discontinued in the third quarter of 2015) and heart failure, and research-related manufacturing for vepoloxamer and AIR001. These expenses consisted primarily of CRO and CMO expenses, clinical study-related consulting and study site expenses.

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The following table summarizes our consolidated R&D expenses by type for each of the periods listed and their respective percent of our total R&D expenses for 2016 and 2015 (in thousands, except for percentages):

	Years Ended December 31,			
	2016	%	2015	%
External clinical study fees and expenses	\$10,765	52 %	\$14,089	50 %
External nonclinical study fees and expenses	5,375	26 %	9,519	34 %
Personnel costs	3,759	18 %	4,058	14 %
Share-based compensation expense	894	4 %	598	2 %
Total	\$20,793	100 %	\$28,264	100 %

R&D expenses decreased by \$7.5 million, or 26.4%, to \$20.8 million for the year ended December 31, 2016, compared to \$28.3 million for the year ended December 31, 2015. This decrease was due primarily to a \$4.1 million decrease in external nonclinical study fees and expenses, a \$3.3 million decrease in external clinical study fees and expenses, and a \$0.3 million decrease in personnel costs, offset by a \$0.3 million increase in share-based compensation expense.

The \$4.1 million decrease in external nonclinical study fees and expenses resulted primarily from decreases of \$4.7 million in research-related manufacturing costs for vepoloxamer and \$1.5 million related primarily to nonclinical studies of vepoloxamer to support our NDA submission, offset by increases of \$1.9 million in external costs related to preparing the NDA and \$0.2 million in research-related manufacturing costs for AIR001. The \$3.3 million decrease in external clinical study fees and expenses was related

primarily to decreases of \$5.0 million in EPIC study costs (as patient enrollment was completed in February 2016) and \$0.5 million in costs for our discontinued Phase 2 study of vepoloxamer in ALI, offset by increases of \$1.3 million in costs for our Phase 2 study of vepoloxamer in heart failure and \$0.9 million in costs related to AIR001 clinical study expenses. The \$0.3 million decrease in personnel costs was due primarily to reductions in our workforce that occurred in the fourth quarter of 2016.

Selling, General and Administrative Expenses. In 2016 and 2015, our SG&A expenses primarily consisted of employee salaries and benefits, share-based compensation expense, facility lease and insurance costs, and professional and consulting fees for accounting, legal, investor relations, market strategy and research, human resources, facilities, and internal systems support.

SG&A expenses decreased by \$1.7 million, or 14.8%, to \$9.3 million for the year ended December 31, 2016, compared to \$11.0 million for the year ended December 31, 2015. This decrease was due primarily to a \$1.0 million decrease in personnel costs and a \$0.5 million decrease in professional and consulting fees. Personnel costs for 2015 include \$0.4 million of severance expense and \$0.3 million of share-based compensation expense resulting from the termination of employment of our former president and chief operating officer in February 2015 and the acceleration of stock option vesting pursuant to the terms of his option agreements.

Transaction-Related Expenses. Transaction-related expenses of \$0.3 million for the year ended December 31, 2016 consisted primarily of professional financial and legal advisor fees associated with evaluating strategic opportunities after determining that the Phase 3 study of vepoloxamer did not meet its primary efficacy endpoint and negotiating the merger agreement with Savara. There were no transaction-related expenses for the year ended December 31, 2015.

IPR&D Impairment Expense. We incurred an impairment expense of \$6.0 million for the year ended December 31, 2016 due to our determination that the carrying amount of our vepoloxamer-related IPR&D exceeded its estimated fair value at December 31, 2016. See Note 4, "Goodwill and IPR&D," of the Notes to Consolidated Financial Statements appearing in this report for a discussion of our IPR&D impairment analysis.

Interest Expense. Interest expense for the year ended December 31, 2016 was \$2.1 million, compared to interest expense of \$0.6 million for the year ended December 31, 2015. The variance of \$1.5 million is attributed to a full year of interest expense on our debt facility in 2016, including nine months on a \$15.0 million principal balance, versus four months of interest expense on our debt facility in 2015, as well as increased amortization of debt issuance costs as a result of a change in the amortization schedule of such costs due to prepayment of \$10.0 million of the principal balance in October 2016.

Net Loss. Net loss was \$36.1 million, or \$0.17 per share (basic and diluted), for the year ended December 31, 2016, compared to a net loss of \$39.8 million, or \$0.25 per share (basic and diluted), for the year ended December 31, 2015.

Income Tax Benefit. In connection with recognizing an impairment loss on our vepoloxamer-related IPR&D, we reduced our deferred tax liability associated with the vepoloxamer-related IPR&D from \$2.6 million to \$0.2 million and recorded \$2.4 million as an income tax benefit.

Results of Operations – Comparison of 2015 and 2014

Revenue. We recognized no revenue for the years ended December 31, 2015 and 2014.

Operating Expenses. The following table illustrates the types of operating expenses we incurred in 2015 and 2014 and their respective percent of our total operating costs for those periods:

	Operating Expenses		Years Ended December 31,	
	2015		2014	
Research and development	72	%	66	%
Selling, general and administrative	28	%	33	%
Transaction-related expenses	—		1	%
Depreciation and amortization	0	%	0	%
Total operating expenses	100	%	100	%

R&D Expenses. In 2015, our most significant R&D expenses were external costs associated with the EPIC study, our Phase 2 studies of vepoloxamer in ALI and heart failure, and research-related manufacturing for vepoloxamer and AIR001. These expenses consisted primarily of CRO and CMO expenses, clinical study-related consulting and study site expenses. In 2014, our most significant R&D expenses were external costs associated with the EPIC study, the Phase 2 study of vepoloxamer in ALI, and research-related manufacturing for vepoloxamer.

The following table summarizes our consolidated R&D expenses by type for each of the periods listed and their respective percent of our total R&D expenses for 2015 and 2014 (in thousands, except for percentages):

	Years Ended December 31,			
	2015	%	2014	%
External clinical study fees and expenses	\$ 14,089	50 %	\$ 11,158	57 %
External nonclinical study fees and expenses	9,519	34 %	4,451	23 %
Personnel costs	4,058	14 %	3,401	18 %
Share-based compensation expense	598	2 %	425	2 %
Total	\$28,264	100%	\$19,435	100%

R&D expenses increased by \$8.8 million, or 45.4%, to \$28.3 million for the year ended December 31, 2015, compared to \$19.4 million for the year ended December 31, 2014. This increase was due to a \$5.1 million increase in external nonclinical study fees and expenses, a \$2.9 million increase in external clinical study fees and expenses, a \$0.7 million increase in personnel costs and a \$0.2 million increase in share-based compensation expense.

The \$5.1 million increase in external nonclinical study fees and expenses resulted primarily from increases of: 1) \$2.9 million in research-related manufacturing costs for vepoloxamer, 2) \$1.8 million primarily related to nonclinical toxicology studies of vepoloxamer to support our NDA submission, and 3) \$0.4 million in consulting expenses for vepoloxamer NDA-readiness activities. The \$2.9 million increase in external clinical study fees and expenses was related primarily to increases of \$3.3 million in EPIC study costs and \$0.9 million in costs for our Phase 2 study of vepoloxamer in heart failure, offset by decreases of \$0.8 million in costs for the discontinued Phase 2 study of vepoloxamer in ALI and \$0.5 million in costs related to AIR001 clinical study expenses. The \$0.7 million increase in personnel costs resulted primarily from additional regulatory, clinical operations, and research-related manufacturing staff hired in 2015.

Selling, General and Administrative Expenses. In 2015 and 2014, our SG&A expenses primarily consisted of employee salaries and benefits, share-based compensation expense, facility lease and insurance costs, and professional and consulting fees for accounting, legal, investor relations, market strategy and research, human resources, facilities, and internal systems support.

SG&A expenses increased by \$1.5 million, or 15.6%, to \$11.0 million for the year ended December 31, 2015, compared to \$9.5 million for the year ended December 31, 2014. This increase was due primarily to a \$0.7 million increase in professional and consulting fees and a \$0.5 million increase in personnel costs. Personnel costs for 2015 include \$0.4 million of severance expense and \$0.3 million of share-based compensation expense resulting from the termination of employment of our former president and chief operating officer in February 2015 and the acceleration of stock option vesting pursuant to the terms of his option agreements.

Transaction-Related Expenses. There were no transaction-related expenses for the year ended December 31, 2015. Transaction-related expenses of \$0.3 million for the year ended December 31, 2014 consisted primarily of legal fees associated with the acquisition of Aires.

Interest Expense. Interest expense for the year ended December 31, 2015 was \$603,000, \$601,000 of which was related to interest expense on our debt facility, which we entered into in August 2015. There was no interest expense in the year ended December 31, 2014.

Other Income/(Expense), Net. Other income/(expense), net for the year ended December 31, 2015 was negligible. Other income, net for the year ended December 31, 2014 was \$0.5 million, which was due primarily to a \$0.5 million

bargain purchase gain associated with the acquisition of Aires.

Net Loss. Net loss was \$39.8 million, or \$0.25 per share (basic and diluted), for the year ended December 31, 2015, compared to a net loss of \$28.7 million, or \$0.23 per share (basic and diluted), for the year ended December 31, 2014.

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IPR&D Impairment and Associated Decrease in Deferred Income Tax Liability

In accordance with our accounting policy related to acquired IPR&D, we test for impairment of acquired IPR&D annually as of September 30, and between annual tests if we become aware of an event or change in circumstances that would indicate its carrying value may be impaired. In October 2016, we engaged an investment bank as a financial adviser in connection with evaluating strategic opportunities for our company, including monetization of our vepoloxamer-related assets. At that time, we had determined to discontinue all clinical development of vepoloxamer in order to focus on the AIR001 program, but we continued to support a grant-funded nonclinical study of vepoloxamer in ischemic stroke. In connection with our annual impairment testing, we determined that vepoloxamer still had technological feasibility and we continue to believe that is the case. However, our evaluation of strategic opportunities during the fourth quarter of 2016 indicated that the carrying value of the vepoloxamer-related acquired IPR&D, which was \$6.5 million at September 30, 2016, exceeded its fair value. We identified limited opportunities to monetize the vepoloxamer-related assets and our proposed merger partner, Savara, did not ascribe any significant value to those assets in negotiation of the merger agreement and agreed to allow us to continue to seek to monetize those assets during the pre-closing period of the proposed merger, including through a sale or other transfer of all or substantially all of the assets. These changes in circumstances indicated to us that the carrying value of the IPR&D may be impaired. Accordingly, we performed a quantitative assessment of the vepoloxamer-related acquired IPR&D as of December 31, 2016. As discussed in Note 4, "Goodwill and IPR&D," of the Notes to Condensed Consolidated Financial Statements appearing in this report, we concluded that, as of December 31, 2016, the carrying value of the vepoloxamer-related acquired IPR&D exceeded its estimated fair value by approximately \$6.0 million. Accordingly, we reduced the carrying value of our IPR&D on our consolidated balance sheet as of December 31, 2016 by \$6.0 million to \$0.5 million. We also decreased our deferred income tax liability by \$2.4 million to reflect the appropriate tax liability at approximately 40% of the fair value of the IPR&D as of December 31, 2016.

Liquidity and Capital Resources

We have a history of annual losses from operations and we anticipate that we will continue to incur losses for at least the next several years. For the years ended December 31, 2016, 2015 and 2014, we incurred losses from operations of \$36.5 million, \$39.4 million and \$29.3 million, respectively. Our cash, cash equivalents and investment securities were \$11.3 million and our working capital was \$7.3 million at December 31, 2016.

We historically have funded our operations principally through proceeds from sales of our equity securities.

In February 2016, we completed an underwritten public offering with gross proceeds of \$8.0 million from the sale and issuance of 29,090,910 units, each consisting of one share of our common stock and one warrant to purchase one share of our common stock. Net proceeds, after deducting underwriting discounts and commissions and other estimated offering expenses, were approximately \$7.3 million. The warrants have an exercise price of \$0.42 per share, are exercisable any time on or before February 16, 2021, subject to certain beneficial ownership limitations.

In November 2014, we completed an underwritten public offering with gross proceeds of \$21.0 million from the sale and issuance of units consisting of shares of our common stock and warrants to purchase our common stock at an exercise price of \$0.75 per share and units consisting of "pre-funded" warrants to purchase shares of our common stock at an exercise price of \$0.01 per share and warrants to purchase shares of our common stock at an exercise price of \$0.75 per share. We issued and sold an aggregate of 30,941,102 shares of our common stock, 13,081,428 pre-funded warrants exercisable for up to 13,081,428 shares, and 22,011,265 warrants exercisable for up to 22,011,265 shares. Net proceeds, after deducting underwriting discounts and commissions and other offering expenses, were \$19.7 million. All of the pre-funded warrants had been exercised by September 30, 2016. The other warrants are outstanding and exercisable at any time on or before November 12, 2019, subject to certain beneficial ownership limitations.

We may receive up to \$18.3 million, \$16.5 million, and \$11.9 million of additional net proceeds from the exercise of warrants issued in the underwritten public offerings we completed in June 2013, November 2014, and February 2016, respectively. However, the timing of the exercise and extent to which any of these warrants are exercised before they expire are beyond our control and depend on a number of factors, including certain beneficial ownership limitations and the market price of our common stock. The exercise prices of these warrants are \$0.65, \$0.75, and \$0.42 per share, respectively. In comparison, the closing sale price of our common stock on March 2, 2017 was \$0.12 per share and we do not expect the holders of the warrants to exercise them unless and until our common stock trades at or above the exercise price of their warrants. In addition, if at the time of exercise there is not an effective registration statement available for the issuance of the shares subject to the warrants, they may be exercised on a “cashless” net issuance basis, in which case we would not receive any proceeds from the exercise of these warrants. In the event of certain fundamental transactions, including a business combination whereby another person or group of persons acquires more than 50% of the outstanding shares of our common stock, the holders of these warrants have the right, upon subsequent exercise of the warrants, to the same amount and kind of consideration as the holder would have been entitled to receive if it had exercised its warrants immediately prior to the transaction. The warrant holders in certain circumstances may also have rights to require our company or any successor entity to purchase the holder’s warrants for cash in an amount equal to the Black Scholes value of the unexercised portion of

the holder's warrants. If we purchase outstanding warrants for cash, it may have a significant adverse impact on our liquidity and capital resources.

In February 2014, we entered into a sales agreement with Cowen and Company, LLC, or Cowen, to sell shares of our common stock, with aggregate gross sales proceeds of up to \$30 million, from time to time, through an "at the market," or ATM, equity offering program, under which Cowen acts as sales agent. We refer to that agreement as the 2014 Sales Agreement. In August 2015, we terminated the 2014 Sales Agreement upon entry into a new sales agreement with Cowen to sell shares of our common stock, with aggregate gross sales proceeds of up to \$30 million, from time to time, through an ATM program. As of December 31, 2016, we had sold and issued an aggregate of 73,003,405 shares at a weighted-average sales price of \$0.40 per share under the ATM programs for aggregate gross proceeds of \$29.4 million and \$28.1 million in aggregate net proceeds, after deducting sales agent commission and discounts and our other offering costs. As of December 31, 2016, approximately, \$18.0 million remains available under the ATM program (on a gross proceeds basis).

In 2015, we borrowed \$15.0 million under a debt facility whereby we received proceeds of approximately \$14.8 million, net of fees. The debt facility is governed by a loan and security agreement, as amended, among our company, Hercules Technology III, L.P., and Hercules Capital, Inc. (formerly known as Hercules Technology Growth Capital, Inc.), together referred to as Hercules. During the three months ended September 30, 2016, the top-line results of the Phase 3 clinical study of vepoloxamer triggered a prepayment provision under the loan and security agreement requiring us to prepay to Hercules \$10.0 million of the principal balance of the loan and any accrued but unpaid fees and expenses (referred to as the Second Advance Prepayment). We made the Second Advance Prepayment on October 3, 2016. We are required to repay the remaining principal balance in equal monthly installments of principal and interest payments on the first business day of each month through the scheduled maturity date of January 1, 2019. The principal balance as of March 2, 2017 was \$3.0 million.

Because the proposed merger with Savara would result in a change in control of our company under the loan and security agreement with Hercules, triggering immediate repayment of the outstanding amount of all principal, accrued interest, accrued, unpaid fees and expenses, together with a prepayment charge of 2% of the principal balance and an end of term charge of \$712,500 (referred to as the Change in Control Prepayment Provisions), in March 2017, we entered into an amendment to the loan and security agreement whereby Hercules agreed that the proposed merger with Savara would not trigger the Change in Control Repayment Provisions and that the loan would remain in place upon its existing terms, including the January 1, 2019 scheduled maturity date, following the consummation of the proposed merger, provided the transaction is completed on or before April 30, 2017. However, beginning on the effective date of the amendment, the combined company will be required to maintain (a) at least \$4 million of cash unless and until our company, Savara or the combined company raise at least \$6 million in net cash proceeds from equity and/or subordinated debt financings on or before April 30, 2017 and (b) at least \$2 million of cash unless and until our company, Savara or the combined company raise at least \$20 million in net cash proceeds from equity and/or subordinated debt financings and/or other financing sources approved by Hercules (including grant amounts) on or before August 31, 2017. This amendment to the loan and security agreement will become effective only upon consummation of the proposed merger. The combined company's failure to comply with the minimum cash requirements set forth in the amendment would be an event of default, providing Hercules with the right to require immediate repayment in full of the loan and to exercise other remedies against the combined company, including those described below. In consideration for the amendment and the consents and waivers provided therein by Hercules, we paid an amendment fee of \$50,000 to Hercules upon execution of the amendment. In addition, we have entered into a third amendment of our warrant agreement with Hercules, pursuant to which, as of the date the amendment to the loan and security agreement becomes effective, the warrant exercise price, which currently is \$0.275 per share, will be reduced to the lesser of (a) \$0.10 per share and (b) if the closing market price of our common stock is lower than \$0.10 per share for three consecutive days between January 6, 2017 and the date of the consummation of the merger, the lowest three-day volume-weighted average price of our common stock during that

period.

See Note 9, "Debt Facility," of the Notes to Condensed Consolidated Financial Statements in this report for additional information regarding our debt facility with Hercules. Our obligations under our agreement with Hercules are secured by substantially all of our assets other than our intellectual property, but including proceeds from the sale, licensing or other disposition of our intellectual property. Our intellectual property is subject to negative covenants, which, among other things, prohibit us from selling, transferring, assigning, mortgaging, pledging, leasing, granting a security interest in or otherwise encumbering our intellectual property, subject to limited exceptions. The agreement includes a number of other restrictive covenants that may limit our ability to raise capital through other debt or equity financing. The debt facility also includes events of default, the occurrence and continuation of which would provide Hercules with the right to exercise remedies against us and the collateral securing our indebtedness, which include declaring payment of all or any part of the debt, together with an end of term charge of \$712,500 and a prepayment charge of 1% or 2% of the then outstanding principal balance, immediately due and payable. These events of default include, among other things, our failure to pay any amount due on the due date, our breach or default in the performance of any covenant under the debt facility, our insolvency, the attachment, seizure, or filing of a levy against our assets or a judgment entered against us in an amount greater than \$250,000, the occurrence of any default under certain other indebtedness, and, subject to limited exceptions, the occurrence of an event or circumstance that would reasonably be expected to have a material adverse effect on our business,

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operations, assets or financial condition, our ability to repay our indebtedness in accordance with the terms of the debt facility, or on the collateral securing our indebtedness.

In 2016, we entered into an agreement with Duke University on behalf of its Duke Clinical Research Institute, which is the coordinating center for the INDIE-HFpEF study of AIR001, which agreement requires that we provide test material (AIR001 and placebo), drug delivery devices (nebulizers), regulatory and technical support, and up to approximately \$3 million of financial support to Duke for the performance of the clinical study. The financial support payments are tied to achievement of study-related milestones. We currently anticipate that approximately \$2.3 million in milestone payments will be achieved in 2017 and an additional \$0.1 million during the first quarter of 2018.

Our merger agreement with Savara provides that, immediately following the consummation of the merger, the executive officers of the combined company will be designated by Savara and we do not anticipate that any of our current executive officers will continue to serve as executive officers of the combined company. We also anticipate the termination of employment of our other two full-time employees in connection with the consummation of the merger. As a result, and in accordance with the Executive Severance Agreements between us and each of our current executive officers and the severance arrangements for our non-officer employees approved by our board of directors, we expect to make cash severance payments to our existing employees totaling approximately \$1.8 million on or about the date the merger is completed. In addition, if the merger is consummated on or before July 6, 2017, we expect to make cash bonus payments totaling approximately \$156,000 to our existing employees on or about the date the merger is completed. Please see Part III, Item 11, "Executive Compensation," of this report for additional discussion of severance and bonus arrangements with our executive officers.

We have incurred, and expect to incur additional, significant transaction-related expenses in connection with negotiating and executing the merger agreement with Savara and completing the transactions contemplated by the merger agreement. Transaction-related expenses, which include legal, accounting and financial advisor fees, tail insurance premiums and other service provider costs, are currently estimated to total approximately \$2.6 million. We incurred \$0.3 million of these costs during the fourth quarter of 2016 and recorded that amount as transaction-related expenses on our consolidated statements of operations and comprehensive loss. As of December 31, 2016, \$0.2 million of these costs were accrued on our consolidated balance sheet. We expect to incur the remainder of the anticipated transaction-related expenses in the first half of 2017.

For a discussion of our liquidity and capital resources outlook, see "Management Outlook" below.

The following table sets forth a summary of the primary sources and uses of cash and cash equivalents for each of the years presented below (in thousands):

	Years Ended December 31,		
	2016	2015	2014
Net cash (used in) provided by:			
Operating activities	\$(37,267)	\$(32,949)	\$(24,645)
Investing activities	\$15,199	\$3,395	\$481
Financing activities	\$7,558	\$16,798	\$34,291
Net (decrease)/increase in cash and cash equivalents	\$(14,510)	\$(12,756)	\$10,127

Operating activities. Net cash used in operating activities in 2016 was \$37.3 million and consisted primarily of a net loss of \$36.1 million adjusted for non-cash items, including impairment of IPR&D of \$6.0 million, a decrease for the

related income tax benefit of \$2.4 million, share-based compensation expense of \$2.6 million, amortization of debt issuance costs and debt discount of \$1.0 million and a net decrease of \$8.6 million due to changes in assets and liabilities. Net cash used in operating activities in 2015 was \$32.9 million and consisted primarily of a net loss of \$39.8 million adjusted for non-cash items, including share-based compensation expense of \$2.7 million, a net increase of \$3.9 million due to changes in assets and liabilities, and \$0.2 million of amortization of debt issuance costs and debt discount. Net cash used in operating activities in 2014 was \$24.6 million and consisted primarily of a net loss of \$28.7 million adjusted for non-cash items, including share-based compensation expense of \$2.0 million, a net increase of \$2.4 million due to changes in assets and liabilities, offset by a gain on bargain purchase for the Aires acquisition of \$0.5 million.

Investing activities. Net cash provided by investing activities was \$15.2 million in 2016, \$3.4 million in 2015 and \$0.5 million in 2014. Net cash provided by investing activities has fluctuated significantly from period to period primarily due to the timing of purchases and maturities of investment securities, as well as \$3.5 million in cash obtained in our acquisition of Aires in 2014.

Financing activities. Net cash provided by financing activities was \$7.6 million in 2016, \$16.8 million in 2015 and \$34.3 million in 2014. Net cash provided by financing activities in 2016 consisted of net proceeds of \$11.5 million from sales of our common stock under the ATM program, net proceeds of \$7.3 million from an underwritten public offering of our equity securities in

February 2016 and net proceeds of \$0.5 million from warrant exercises, offset primarily by payments of \$11.7 million on our debt facility. Net cash provided by financing activities in 2015 consisted of net proceeds of \$14.8 million under our debt facility and \$2.0 million from sales of our shares of common stock under the ATM program. Net cash provided by financing activities in 2014 consisted of net proceeds of \$19.7 million from an underwritten public offering of our equity securities completed in November 2014 and net proceeds of \$14.6 million from sales of our common stock under the ATM program.

Contractual Obligations

The following is a summary of our long-term contractual obligations as of December 31, 2016 (in thousands):

	Total	Less than 1 year	1 - 3 years	3 - 5 years	More than 5 years
Long-term debt obligation with Hercules	\$4,059	\$1,521	\$2,538	\$—	\$—
Payments to Duke University relating to					
INDIE-HFpEF clinical study of AIR001	2,350	2,250	100	—	—
Capital lease obligations	29	10	19	—	—
Operating lease obligations	1,830	489	1,104	237	—
Total	\$8,268	\$4,270	\$3,761	\$237	\$—

Management Outlook

Subject to approval of our stockholders and Savara's stockholders and satisfaction or waiver of the other conditions to closing, we expect the proposed merger will be completed in the second quarter of 2017. If the proposed merger does not close, we may elect to, among other things, attempt to complete another strategic transaction like the proposed merger, attempt to sell or otherwise dispose of our various assets, or continue to operate our business, focusing on advancing the development of AIR001. If our board of directors decides to dissolve our company and liquidate our assets, we would be required to pay all of our debts and contractual obligations, and to set aside certain reserves for potential future claims, and there can be no assurance as to the amount or timing of available cash left to distribute to our stockholders after paying our debts and other obligations and setting aside funds for potential future claims.

Based on our projected capital needs to continue to operate our business if we do not complete the proposed merger with Savara, our current cash, cash equivalents and investment securities and working capital will not be sufficient to fund our operations for the next 12 months and our ability to raise additional capital as needed is uncertain. We expect that our working capital as of December 31, 2016 will be sufficient to fund our operations into the second quarter of 2017. We are focused on managing our operating expenses and maintaining adequate cash to run our business until we close the proposed merger. In addition to managing our operating expenses, we are exploring opportunities to monetize our vepoloxamer-related assets prior to consummation of the merger. However, we may not be successful in completing the merger with Savara, monetizing our vepoloxamer-related assets, or raising sufficient additional capital to continue to operate our business. These uncertainties raise substantial doubt about our ability to continue as a going concern.

Estimates of the period of time through which our current financial resources will be adequate to support our operations are forward-looking statements based on significant assumptions. We could utilize our financial resources sooner than we currently expect. Forward-looking statements involve a number of risks and uncertainties and actual results could differ materially if the assumptions on which we have based our forward-looking statements prove to be wrong. Factors that will affect our operating expenses and future capital requirements include, but are not limited to:

- the extent of expenses incurred in connection with seeking stockholder approval of the proposed merger and completing the transactions contemplated by our merger agreement with Savara;
- our ability to manage our operating costs;
- the scope and nature of activities we pursue to advance development of our product candidates, including clinical and nonclinical studies and research-related manufacturing activities;
- delays in commencement and completion of clinical and nonclinical studies of our product candidates and the extent to which results are negative or inconclusive;
- resources allocated to pursue strategic opportunities for our vepoloxamer-related assets, or, if we do not consummate the proposed merger with Savara, to pursue potential financing transactions or strategic opportunities for all of our assets, and the nature of any such transaction, if executed; and

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our ability to avoid an event of default under our loan agreement with Hercules that would accelerate repayment of all or part of our obligations under the agreement.

If we are unable to raise sufficient additional capital as needed, we may further reduce our operations and we may also be compelled to repay all of our outstanding debt to Hercules and/or sell certain assets, including intellectual property assets, for less than what we believe their value may be under other circumstances, any of which would have a material and adverse effect on our financial condition and ability to pursue our business strategy.

Recent Accounting Pronouncements

See Note 2, “Summary of Significant Accounting Policies — Recent Accounting Pronouncements,” of the Notes to Consolidated Financial Statements in this report for a discussion of recent accounting pronouncements and their effect, if any, on us.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We have market risk exposure related to our cash, cash equivalents and investment securities. We invest our excess cash in FDIC-insured certificates of deposit. Changes in interest rates affect the interest income we earn on our investments and therefore impacts our cash flows and results of operations.

We do not believe that our cash, cash equivalents and investment securities have significant risk of default or illiquidity. While we believe our cash and cash equivalents do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. In addition, we maintain significant amounts of cash and cash equivalents at one or more financial institutions that are in excess of federally insured limits.

We also have interest rate exposure as a result of our debt facility with Hercules. As of December 31, 2016, the outstanding principal amount of the term loan was \$3.3 million. The outstanding principal under the loan accrues interest at a rate equal to the greater of (i) 8.95% plus the prime rate as reported from time to time in The Wall Street Journal minus 3.25%, and (ii) 8.95%. Changes in the prime rate may therefore affect our interest expense associated with our secured term loan.

If a 10% change in interest rates from the interest rates on December 31, 2016 were to have occurred, this change would not have had a material effect on the value of our investment portfolio or on our interest expense obligations with respect to outstanding borrowed amounts.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material effect on our results of operations during the periods presented.

Item 8. Financial Statements and Supplementary Data.

The consolidated financial statements and supplementary financial information required by this item are filed with this report as described under Item 15.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to provide reasonable assurance that information required to be disclosed by us in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can only provide reasonable assurance of achieving the desired control objectives, and in reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we have evaluated the effectiveness of our disclosure controls and procedures (as defined under Exchange Act Rule 13a-15(e)) as of December 31, 2016. Based on that evaluation, our principal executive officer and principal financial officer have concluded that as of December 31, 2016 these disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rule 13a-15(f). Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2016 based on the framework in Internal Control — Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on our evaluation under the framework in Internal Control — Integrated Framework (2013), our management concluded that our internal control over financial reporting was effective as of December 31, 2016.

The effectiveness of our internal control over financial reporting as of December 31, 2016 has been audited by Mayer Hoffman McCann P.C., an independent registered public accounting firm, as stated in their report, which appears on page F 3 of this annual report.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting identified in connection with the evaluation required by Exchange Act Rules 13a-15(d) and 15d-15(d) that occurred during the fiscal quarter ended December 31, 2016 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

Fifth Amendment to Loan and Security Agreement and Third Amendment to Warrant Agreement with Hercules

On March 3, 2017, we entered into a fifth amendment to our Loan and Security Agreement, dated as of August 11, 2015, with Hercules Technology III, L.P. and Hercules Capital, Inc. (formerly known as, Hercules Technology Growth Capital, Inc.) (together referred to as Hercules), as previously amended by the First Amendment to Loan and Security Agreement dated as of September 28, 2015, the Second Amendment to Loan and Security Agreement effective as of December 31, 2015, the Third Amendment to Loan and Security Agreement effective as of February 25, 2016, and the Fourth Amendment to Loan and Security Agreement effective as of July 22, 2016 (collectively

referred to as the Loan Agreement). This amendment was contemplated under our merger agreement with Savara because the proposed merger otherwise would result in a change in control of our company under the Loan Agreement, triggering immediate repayment of the outstanding amount of all principal, accrued interest, accrued, unpaid fees and expenses, together with a prepayment charge of 2% of the principal balance and an end of term charge of \$712,500 (referred to as the Change in Control Prepayment Provisions).

Pursuant to the amended Loan Agreement, provided that our merger agreement with Savara is not terminated or amended in a manner that adversely affects the agreements and understandings in the amended Loan Agreement and the proposed merger is consummated on or before April 30, 2017, Hercules consented to the transactions contemplated in our merger agreement with Savara and agreed that the proposed merger would not trigger the Change in Control Repayment Provisions. Therefore, the loan would remain in place upon its existing terms, including the January 1, 2019 scheduled maturity date, following the consummation of the merger. However, the amended Loan Agreement includes a minimum cash covenant such that, beginning on the effective date of the amendment, the combined company will be required to maintain (a) at least \$4 million of cash unless and until our company, Savara or the combined company raise at least \$6 million in net cash proceeds from equity and/or subordinated debt financings on or before

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April 30, 2017 and (b) at least \$2 million of cash unless and until our company, Savara or the combined company raise at least \$20 million in net cash proceeds from equity and/or subordinated debt financings and/or other financing sources approved by Hercules (including grant amounts) on or before August 31, 2017. This amendment to the Loan Agreement will become effective only upon consummation of the proposed merger.

In consideration for the amendment to the Loan Agreement and the consents and waivers provided therein by Hercules, we paid an amendment fee of \$50,000 to Hercules upon execution of the amendment. In addition, on March 3, 2017, we entered into a third amendment to our Warrant Agreement with Hercules Technology III, L.P., dated as of August 11, 2015, as previously amended by the First Amendment to Warrant Agreement dated as of September 28, 2015 and the Second Amendment to Warrant Agreement dated as of February 25, 2016 (collectively referred to as the Warrant Agreement), pursuant to which, as of the date the amendment to the Loan Agreement becomes effective, the warrant exercise price, which currently is \$0.275 per share, will be reduced to the lesser of (a) \$0.10 per share and (b) if the closing market price of our common stock is lower than \$0.10 per share for three consecutive days between January 6, 2017 and the date of the consummation of the merger with Savara, the lowest three-day volume-weighted average price of our common stock during that period.

We offered and sold the securities described above to Hercules in reliance upon the exemption from the registration requirements of the Securities Act of 1933, as amended, or the Securities Act, provided by Section 4(a)(2) of the Securities Act. We relied on this exemption based in part on representations made to us by Hercules, including Hercules' intention to acquire the securities for investment only and not with a view to, or a present intention of, selling or distributing any part thereof in violation of applicable laws, and Hercules' status as an "accredited investor," as such term is defined in Rule 501 of Regulation D promulgated under the Securities Act. Appropriate legends were affixed to securities certificates issued in these transactions. Hercules had adequate access to information about our company.

PART III

Item 10. Directors, Executive Officers and Corporate Governance. Board of Directors and Executive Officers

Our amended and restated certificate of incorporation and amended and restated bylaws, each as amended to date, provide that each director elected or appointed to our board of directors shall hold office until the next annual meeting of our stockholders following such election or appointment and until the director's successor is elected and qualified, or until the director's earlier resignation or removal. Our bylaws provide that vacancies on our board of directors, including those resulting from an increase in the authorized number of directors, may be filled by a majority of the remaining directors, even if less than a quorum, or by a sole remaining director. Any director appointed as a result of a vacancy holds office until the next annual meeting of stockholders and until a successor is elected and qualified, or until that director's earlier resignation or removal. Pursuant to our bylaws, the authorized number of directors may be not less than three nor more than nine, with the exact number, which currently is five, to be fixed by resolutions adopted from time to time by our board of directors.

Set forth below are the names, ages as of March 2, 2017, board committee assignments, if applicable, and certain biographical information about our directors and executive officers. Additionally, information about the specific experience, qualifications, attributes or skills that let to our board of directors' conclusion that each director listed below should serve as a director is set forth below.

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Name	Age	Title	Board Committee Membership
			<ul style="list-style-type: none"> • Audit Committee • Compensation Committee • Nominating & Governance Committee
Matthew Pauls	46	Chair of the Board	
Brian M. Culley			
	45	Chief Executive Officer and Director	<ul style="list-style-type: none"> • None • Compensation Committee (Chair)
Howard C. Dittrich	63	Director	<ul style="list-style-type: none"> • Nominating & Governance Committee (Chair) • Audit Committee
Peter Greenleaf	47	Director	<ul style="list-style-type: none"> • Compensation Committee • Audit Committee (Chair)
David A. Ramsay	52	Director	<ul style="list-style-type: none"> • Nominating & Governance Committee
Brandi L. Roberts			
		Chief Financial Officer & Senior Vice President	
	43	President	N/A

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Edwin L. Parsley

56 Chief Medical Officer & Senior Vice President N/A

Shana Hood

40 General Counsel, Vice President & Secretary N/A

Matthew Pauls. Mr. Pauls joined our board of directors in October 2015 and has served as chair of the board since March 2016. Mr. Pauls currently serves as President and Chief Executive Officer of Strongbridge Biopharma plc (NASDAQ: SBBP), a biopharmaceutical company focused on therapies that target rare diseases, a position he has held since August 2014. He also has served as a member of the board of directors of Strongbridge since September 2015. Prior to Strongbridge, from April 2013 to August 2014, Mr. Pauls was Chief Commercial Officer of Insmed, Inc., a publicly traded global biopharmaceutical company focused on rare diseases. Prior to Insmed, Mr. Pauls worked at Shire Pharmaceuticals, a global specialty biopharmaceutical company, from 2007 to April 2013, most recently as Senior Vice President, Head of Global Commercial Operations from May 2012 to April 2013. Earlier in his career, from 1997 to 2007, Mr. Pauls held senior positions at Bristol-Myers Squibb in Brand Management and Payor Marketing and at Johnson & Johnson in various U.S. and global commercial roles. Mr. Pauls holds B.S. and M.B.A. degrees from Central Michigan University and a J.D. from Michigan State University College of Law. Mr. Pauls' leadership experience and extensive commercialization, strategic planning and operations experience in the biopharmaceutical industry and particularly with therapies for rare diseases are among the qualifications that led our board of directors to conclude that Mr. Pauls should serve as a member of our board.

Brian M. Culley. Mr. Culley has served as our Chief Executive Officer since February 2010 and as a member of our board of directors since December 2011. He has served as our principal executive officer since February 2009. Previously, from January 2007 to February 2010, he served as our Chief Business Officer and Senior Vice President, from February 2006 to January 2007, he served as our Senior Vice President, Business Development, and, from December 2004 to February 2006, he served as our Vice President, Business Development. From 2002 until 2004, Mr. Culley managed all strategic collaborations and licensing agreements for Immusol, Inc. in San Diego, where his most recent title was Director of Business Development and Marketing. From 1999 until 2000, he was a licensing and marketing associate at the University of California, San Diego, department of technology transfer & intellectual property services and from 1996 to 1999, he was a research associate for Neurocrine Biosciences, Inc. Mr. Culley has more than 20 years of experience in the life science industry. He received a B.S. in biology from Boston College, a masters in biochemistry from the University of California, Santa Barbara and an M.B.A. from The Johnson School of Business at Cornell University. Mr. Culley's extensive experience with our company and our board of directors' belief that our Chief Executive Officer should serve on the board of directors, as well as Mr. Culley's substantial business experience, leadership skills and scientific background, led our board of directors to conclude that Mr. Culley should serve as a director for our company.

Howard C. Dittrich. Dr. Dittrich has served as a director since June 2014. A cardiologist with more than 20 years of experience in cardiac therapeutic research and clinical development, Dr. Dittrich joined Frazier Healthcare Partners in January 2016 as an Entrepreneur-in-Residence and also began serving as Chief Medical Officer of Hawkeye Therapeutics, a biotechnology company formed by Frazier. In addition, he currently serves as President and a member of the board of directors of Advanced Endovascular Therapeutics, Inc., a privately-held biotechnology company that he co-founded in August 2015. Additionally, Dr. Dittrich co-founded and from March 2014 until February 2016 served as Chairman of the board of directors of IOWA Approach Inc., a privately-held company developing atrial fibrillation ablation technology. He also is an Adjunct Professor of Medicine at the University of Iowa Carver College of Medicine and, since January 2012, has served as Chair of the board of directors of the François M. Abboud Cardiovascular Research Center at the University of Iowa Carver College of Medicine. He also serves as a consultant to other privately-held life science companies. From November 2011 to November 2015, Dr. Dittrich served as Chief Medical Officer of Laguna Pharmaceuticals, a privately-held biopharmaceutical company, first as a consultant and,

beginning in February 2015, as an employee. From April 2012 to July 2014, he served as Chief Medical Officer of Sorbent Therapeutics, a privately-held biopharmaceutical company that commenced liquidation proceedings through an assignment for the benefit of creditors under California law in July 2014. Previously, from 2003 until it was acquired by Merck & Co., Inc. in September 2007, Dr. Dittrich served as Chief Medical Officer and Senior Vice President of Clinical and Regulatory Affairs of NovaCardia, Inc., a clinical-stage pharmaceutical company focused on cardiovascular diseases, and, from September 2007 to June 2011, he co-founded and served as Chief Medical Officer of Sequel Pharmaceuticals, Inc., a privately-held pharmaceutical company spun out from NovaCardia following its acquisition by Merck. Prior to NovaCardia, from 1996 to 2002, Dr. Dittrich held executive positions overseeing clinical development and regulatory affairs at Molecular Biosystems, Inc. and Alliance Pharmaceutical Corp. From 1984 to 1996, he was a full-time faculty member of the Department of Medicine at the University of California, San Diego (UCSD) and, from 1996 to 2011, he served part-time as clinical professor of medicine at UCSD. Dr. Dittrich holds a B.S. degree from the University of Iowa and an M.D. from the University of Iowa Carver College of Medicine. He completed his residency in internal medicine and clinical fellowship in cardiology at UCSD. Dr. Dittrich's extensive medical and pharmaceutical development expertise, including his background in the clinical practice of medicine, clinical research and development, and regulatory affairs and his experience with the successful development of medicinal products, are among the attributes that led our board of directors to conclude that he should serve as a member of our board.

Peter Greenleaf. Mr. Greenleaf has served as a director since November 2015. Mr. Greenleaf currently serves as Chief Executive Officer and as a member of the board of directors of Sucampo Pharmaceuticals, Inc. (NASDAQ: SCMP), positions he has held since March 2014. Sucampo is focused on the development and commercialization of medicines to meet major unmet medical needs of patients worldwide. Prior to joining Sucampo, from June 2013 to February 2014, Mr. Greenleaf served as Chief Executive Officer and a member of the board of directors of Histogenics Corporation, a regenerative medicine company. Prior to joining Histogenics, from 2006 to 2013, Mr. Greenleaf was employed by MedImmune LLC, the global biologics arm of AstraZeneca, where he most recently served as President. From January 2010 to June 2013, Mr. Greenleaf also served as President of MedImmune Ventures, a wholly owned venture capital fund within the AstraZeneca Group. Prior to serving as President of MedImmune, Mr. Greenleaf was Senior Vice President, Commercial Operations of the company, responsible for its commercial, corporate development and strategy functions. Mr. Greenleaf has also held senior commercial roles at Centocor Biotech, Inc. (now Janssen Biotechnology, Johnson & Johnson) from 1998 to 2006, and at Boehringer Mannheim G.m.b.H. (now Roche Holdings) from 1996 to 1998. Mr. Greenleaf currently serves as a member of the board of directors of Mirna Therapeutics, Inc., a clinical-stage biopharmaceutical company developing oncology therapeutics, and as a member of the board of directors of the Biotechnology Industry Organization (BIO), where he serves on the Governing Boards of the Emerging Companies and Health Sections. Mr. Greenleaf also chairs the Maryland Venture Fund Authority, whose vision is to oversee implementation of InvestMaryland, a public-private partnership to spur venture capital investment in the state. Mr. Greenleaf earned a M.B.A. degree from St. Joseph's University and a B.S. degree from Western Connecticut State University. Mr. Greenleaf's leadership experience and extensive commercialization, strategic planning, and drug development experience in the biopharmaceutical industry are among the characteristics that led our board of directors to determine that he should serve as a director for our company.

David A. Ramsay. Mr. Ramsay has served as a director since June 2011. Mr. Ramsay served as Chief Financial Officer of Halozyme Therapeutics, Inc. (NASDAQ: HALO), a biotechnology company developing and commercializing novel oncology therapies, from May 2013 until his retirement in July 2015 and from 2003 to May 2009. He also served as Halozyme's Vice President, Corporate Development from May 2009 to May 2013. Mr. Ramsay currently provides consulting services to biotechnology companies, both publicly traded and privately-held. From 2000 to 2003, Mr. Ramsay was Vice President, Chief Financial Officer of Lathian Systems, Inc., a provider of technology-based sales solutions for the life science industry. From 1998 to 2000, he was with Valeant Pharmaceuticals International, Inc. (formerly ICN Pharmaceuticals, Inc.), a multinational specialty pharmaceutical company, where he served as Vice President, Treasurer and Director, Corporate Finance. Mr. Ramsay began his career at Deloitte & Touche, where he obtained his CPA license. Mr. Ramsay holds a B.S. in business administration from the University of California, Berkeley and a M.B.A. with a dual major in finance and strategic management from The Wharton School at the University of Pennsylvania. Mr. Ramsay's significant experience as chief financial officer of life science companies, particularly his experiences at Halozyme during its successful development and its commercialization of its first products, and at a large audit and financial advisory firm, are among the qualifications that led are our board of directors to determine that Mr. Ramsay should serve as a director for our company.

Brandi L. Roberts. Ms. Roberts joined our company in March 2011 and currently serves as our Chief Financial Officer and Senior Vice President. She previously served as our Vice President, Finance from March 2011 to January 2013 and from June 2008 to January 2009. From January 2009 to March 2011, Ms. Roberts served as Vice President, Accounting and Corporate Controller of Alphatec Spine, Inc., the wholly-owned operating subsidiary of Alphatec Holdings, Inc., a medical technology company listed on the NASDAQ Global Select Market where she was responsible for managing all accounting activities, including SEC reporting and compliance with Sarbanes-Oxley Act requirements. From June 2007 to June 2008, Ms. Roberts served as Executive Director, Corporate Controller of Artes Medical, Inc., a publicly traded medical technology company, and from September 2005 to June 2007, she served as Director, Finance of Stratagene Corporation, a publicly traded life science company acquired by Agilent Technologies, Inc. in June 2007. Ms. Roberts' experience also includes seven years at Pfizer's laboratories in La Jolla,

California (formerly Agouron), most recently as Director, Finance, and three years with the public accounting firm of PricewaterhouseCoopers LLP. She is a certified public accountant with the State of California. Ms. Roberts received a B.S. in Business Administration from the University of Arizona and an M.B.A. from the University of San Diego.

Edwin L. Parsley. Dr. Parsley has served as our Chief Medical Officer and Senior Vice President since October 2014. He served as our interim Chief Medical Officer in September 2014 and has served as Chief Medical Officer of our wholly-owned subsidiary, Aires Pharmaceuticals, Inc., since we acquired Aires in February 2014. Prior to the acquisition, he had served as Chief Medical Officer of Aires since April 2011. Dr. Parsley joined Aires from Pfizer where he oversaw clinical trials for Revatio® (sildenafil) and consulted across molecules in Pfizer's pulmonary vascular disease portfolio on clinical trial design, conduct and data interpretation from January 2010 to April 2011. Prior to Pfizer, from January 2009 to September 2009, Dr. Parsley worked at CSL Biotherapies as its pulmonary hypertension medical science specialist and, from 2006 to December 2008, at Encysive Pharmaceuticals, Inc. where he most recently served as its Executive Director for Global Medical Affairs and Drug Safety, developing endothelin receptor antagonists for pulmonary hypertension, heart failure, renal failure and resistant hypertension. Dr. Parsley is a practicing physician and certified by the American Board of Internal Medicine in internal medicine, pulmonary disease, critical care medicine and sleep medicine. He earned his D.O. from Oklahoma State University College of Osteopathic Medicine and a B.S. Pharmacy from Southwestern Oklahoma State University. Prior to joining industry, Dr. Parsley was an Assistant Professor of Medicine at the

University of Texas Medical School at Houston and a Medical Director of Medical Intensive Care and Respiratory Therapy Services at Memorial Hermann Hospital in Houston, where he had an active inpatient care and office practice with focus on pulmonary hypertension and fibrosis research. He also worked in the emergency department at Lyndon B. Johnson Hospital, a Harris County Hospital District facility in Houston. In the course of his practice, Dr. Parsley treated patients with a range of acute care needs, including patients with sickle cell disease, heart failure and stroke.

Shana Hood. Ms. Hood has served as our General Counsel and Vice President since January 2016 and as our Secretary since June 2015. Ms. Hood joined our company as Associate General Counsel in February 2010 and was promoted to Vice President, Legal in March 2015 before being promoted to her current position. Prior to joining our company, Ms. Hood was associated with the law firms of DLA Piper LLP (US) from May 2008 to February 2010, Heller Ehrman LLP from February 2003 to April 2008, and Brobeck, Phleger & Harrison LLP, from October 2002 to February 2003, where she specialized in public and private financing transactions, mergers and acquisitions, SEC reporting, and general corporate governance and compliance matters. Ms. Hood is a member of the State Bar of California. She holds a B.S. in commerce from Santa Clara University and a J.D. from the University of San Diego School of Law.

Compliance with Section 16(a) of the Securities Exchange Act of 1934

Our records reflect that all reports which were required to be filed pursuant to Section 16(a) of the Exchange Act during or with respect to the year ended December 31, 2016 were filed on a timely basis.

Code of Ethics

We have adopted a code of ethics that applies to our principal executive officer, principal financial officer, principal accounting officer or persons performing similar functions, as well as all of our other officers, directors and employees. This code of ethics is a part of our code of business conduct and ethics, and is available on our corporate website at www.masttherapeutics.com. We intend to disclose future amendments to, or waivers of, certain provisions of our code of ethics that apply to our principal executive officer, principal financial officer, principal accounting officer or persons performing similar functions on our corporate website within four business days following such amendment or waiver.

Procedures by Which Stockholders May Nominate Directors

There have been no changes to the procedures by which our stockholders may recommend nominees to our board of directors since our last annual report on Form 10-K, including the Part III information incorporated therein.

Audit Committee and Audit Committee Financial Expert

The audit committee of our board of directors is composed of Mr. Ramsay (chair), Mr. Greenleaf and Mr. Pauls and met four times, on a quarterly basis, during the year ended December 31, 2016. Mr. Pauls was appointed to the audit committee in March 2016. Lewis Shuster, who resigned from our board of directors in March 2016, served on the audit committee during 2016 until his resignation. Each current audit committee member, and the former director who served on the audit committee during 2016, satisfies, or satisfied in the case of the former director, the independence standards specified in Rule 10A-3 under the Securities Exchange Act of 1934, as amended, and the other independence standards for audit committee members specified by the NYSE MKT Company Guide. In addition, our board of directors concluded that Mr. Ramsay is an “audit committee financial expert,” as that term has been defined by the SEC.

In accordance with its written charter, the primary purpose of the audit committee is to oversee our accounting and financial reporting processes, including our internal controls system, and audits of our financial statements. The audit committee's responsibilities include: appointing and providing for the compensation of the independent registered public accounting firm to be engaged to prepare and issue an audit report and perform other audit, review or attest services for our company; approving any other permissible non-audit services to be provided to us by the independent auditor; overseeing the work and evaluating the performance of the independent auditor, and, if so determined by the audit committee, terminating and replacing the independent auditor; reviewing and discussing, including with management and the independent auditor, our annual and quarterly financial statements; reviewing any proposed significant changes to our accounting principles and practices; reviewing any material changes to our system of internal control over financial reporting; reviewing management's report on effectiveness of our internal control over financial reporting and, if applicable, our independent auditor's audit of the effectiveness of our internal control over financial reporting; establishing a procedure for receipt, retention and treatment of any complaints or concerns received by us about our accounting, internal accounting controls or auditing matters; reviewing, approving and overseeing any related party transaction that would require disclosure pursuant to Item 404 of Regulation S-K; overseeing the implementation and enforcement of our insider trading policy; and reviewing and evaluating any significant financial risk exposures facing our company and the steps our management has taken to control and monitor such exposures.

A copy of the audit committee's charter, as well as copies of the charters of our board of directors' compensation committee and nominating and governance committee and our corporate governance guidelines, are posted on our corporate website at www.masttherapeutics.com.

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Item 11. Executive Compensation.

Compensation Discussion and Analysis

Introduction

The following Compensation Discussion and Analysis describes the material elements of compensation for our executive officers identified in the Summary Compensation Table below, who are referred to as our “Named Executive Officers” or “NEOs.” The compensation committee of our board of directors assists the board of directors in discharging its responsibilities regarding compensation of our executive officers, including the NEOs. In particular, the compensation committee makes recommendations to the board of directors regarding the corporate goals and objectives relevant to executive compensation, evaluates performance in light of such goals and objectives, and recommends the executives’ compensation levels and components to the board of directors based on such evaluations. In accordance with its charter, at least annually, the compensation committee reviews the elements, amounts, and terms of our executive officers’ compensation. Our Chief Executive Officer attends compensation committee meetings, provides his assessment of corporate and individual performance, and makes recommendations to the compensation committee regarding executive compensation. Other executive officers, including our Chief Financial Officer, also attend compensation committee meetings and provide information regarding corporate goals and performance. In reviewing and making its recommendations to the board of directors, the compensation committee takes into consideration our Chief Executive Officer’s assessment of performance and recommendations regarding goals and objectives and compensation. The compensation committee meets in executive session, outside the presence of our Chief Executive Officer and all other executive officers, to deliberate and determine its recommendations regarding our Chief Executive Officer’s compensation. Our Chief Executive Officer may be present during the deliberation of other officers’ compensation. The compensation committee’s recommendations relating to compensation matters are subject to approval by the board of directors.

For our most recently completed fiscal year (the year ended December 31, 2016), our Named Executive Officers were:

- Brian Culley, our Chief Executive Officer;
- Brandi Roberts, our Chief Financial Officer and Senior Vice President;
- Edwin Parsley, our Chief Medical Officer and Senior Vice President;
- Shana Hood, our General Counsel, Vice President and Secretary;
- R. Martin Emanuele, our former Senior Vice President, Development, who served as our Senior Vice President, Development from April 2011 until October 28, 2016, and began serving as a Research & Development Advisor on a temporary, part-time employment basis on October 31, 2016; and
- Gregory Gorgas, our former Senior Vice President, Commercial, whose employment with us ended on December 28, 2016.

Compensation Philosophy and Objectives

Our executive compensation program is intended to attract and retain our executive officers and to motivate them to increase stockholder value on both an annual and long-term basis. As a clinical-stage biopharmaceutical company, these objectives are to be accomplished primarily by positioning us to maximize our drug product development and regulatory approval efforts and to transform those efforts, over time, into revenues and income from commercialization of and/or strategic collaborations with respect to our product candidates. To that end, our executive compensation packages include a base salary to provide an element of income stability and security that compensates our executive officers for expected day-to-day performance, an annual cash bonus opportunity to incentivize our executive officers to achieve near-term corporate goals that are set by our board of directors and intended to enhance the value of our company, and significant long-term incentive in the form of stock-based compensation to further

align the interests of our executive officers with those of our stockholders, reward long-term value-creation, and increase retention. The components of our executive compensation program also are intended to complement each other and offset risk of overemphasis on short-term goals to the detriment of long-term value creation.

Overview

Our executive compensation program is relatively simple and straightforward, with base salary, annual performance-based cash incentives, and stock options being the principal components. In addition, executive officers generally participate in the same benefit programs as our other full-time employees.

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In reviewing executive compensation for 2016, the compensation committee engaged an independent compensation consultant (as discussed further below) to assist it in evaluating our executive compensation practices, including measuring their competitiveness against an appropriate peer group. For other recent years, including fiscal years 2015 and 2014, the compensation committee did not use a compensation consultant in connection with evaluating and recommending executive compensation, and relied upon the professional and market experience of the compensation committee members, as well as consideration of survey data published by the San Diego Biotechnology Employee Development Coalition. For 2016, the compensation committee determined it was appropriate to target total direct executive compensation (base salary, annual incentive value and long-term incentive value) to the 50th percentile of executive compensation of our peer group. However, the compensation committee also concluded executive compensation may be above or below the 50th percentile based on an executive's responsibilities, experience, performance and internal pay equity considerations.

In determining our peer group and recommending annual performance goals and objectives and stock option awards for 2016, the compensation committee considered that we anticipated a pivotal event for our company in 2016—the completion of enrollment in and announcement of results of a double-blinded Phase 3 clinical study of our lead product candidate. The anticipation of this event and the expectation that, whether positive or negative, the study outcome could result in new strategic opportunities for our company, also, in part, led the compensation committee to consider and recommend executive severance agreements with the NEOs, as discussed further below under “Executive Severance Agreements.” We do not have employment agreements with our executive officers and the executive severance agreements were considered important to enabling the executive officers to identify and evaluate strategic opportunities and business strategy objectively, from the perspective of what is in the best interest of our stockholders, without regard to the potential impact of a transaction on their own job security or personal financial interests.

Pursuant to its charter, the compensation committee has the authority to select and retain the services of compensation consultants to assist it in reviewing and making recommendations regarding executive compensation. In August 2015, the compensation committee engaged Barney & Barney, a Marsh & McLennan Agency LLC Company, to assist it in identifying a group of peer companies to be referenced in the compensation committee's compensation review process for 2016, to conduct an assessment of the competitiveness of our executive compensation against that of the peer companies selected by the compensation committee, and to provide advice as to the structure of our executive compensation program. Before selecting Barney & Barney, the compensation committee conducted an independence assessment in accordance with its charter and the corporate governance standards set forth in the NYSE MKT Company Guide, and concluded that Barney & Barney was an independent adviser and that its work did not raise any conflict of interest.

Executive Compensation Components

Base Salary

The purpose of the base salary component of our executive compensation is to provide a level of income that allows us to attract and retain executive talent and mitigates pressure to focus on stock price performance to the detriment of other important aspects of our business by providing an element of income stability and security. The base salary represents fixed cash compensation recognizing individual performance, scope of responsibility, leadership skills and experience, and it compensates an executive for performing his or her job responsibilities on a day-to-day basis. The base salaries of our executive officers are initially established through arm's-length negotiation at the time of hire. Base salaries are then reviewed at least annually by the compensation committee and may be adjusted to realign with market levels after taking into account individual responsibilities, performance and experience. The compensation committee also evaluates an executive officer's base salary in the context of the executive's other compensation components to ensure that the executive's compensation package is in line with our overall compensation philosophy and objectives as discussed above.

When reviewing base salaries for 2016, the compensation committee considered various data regarding the base salaries of executive officers in comparable positions at other life sciences companies developing specialty pharmaceuticals or biological products as described below under “Factors for Determining 2016 Compensation – Peer Group and Competitive Assessment.” Additional factors included, but were not limited to, company size, market capitalization, stage of development of a company’s lead product candidate, and geographic location. The compensation committee also considered the individual experience level and past performance of each NEO in light of our needs and objectives, as well as whether the NEO was expected to have increased responsibilities relative to the prior year. The compensation committee also reviewed analysis from Barney & Barney to ensure that base salaries would be within the competitive range of other companies in our peer group.

In January 2016, upon recommendation by the compensation committee, our board of directors approved increases of 2.25% to 5.66% to the NEOs' base salaries relative to their 2015 base salaries effective January 1, 2016. The following annual base salaries were determined based on the factors discussed above as well as below under "Factors for Determining 2016 Compensation":

	2016 Salary	Increase over 2015 Salary
Named Executive Officer (\$)		(%)
Brian Culley	428,600	2.25
Brandi Roberts	312,000	4.00
Edwin Parsley	364,575	3.25
Shana Hood	280,000	5.66
R. Martin Emanuele	318,260	2.50
Gregory Gorgas	300,280	5.50

Annual Performance-Based Cash Incentive Plan

Our annual performance-based executive incentive plans, which provide for variable compensation based on performance against annually established objectives, are designed to motivate our executive officers to achieve near-term goals intended to enhance the long-term value of our company without excessive risk taking. In March 2016, upon recommendation of the compensation committee, our board of directors adopted and approved the 2016 Executive Incentive Plan, pursuant to which executive officers were eligible for incentive awards, generally payable in cash, based on achievement of corporate and, potentially, individual performance objectives.

Under the 2016 Executive Incentive Plan, each participant was assigned an incentive target that was expressed as a percentage of his or her annual base salary, with the participant's actual incentive award to be based on the level of achievement of the corporate objectives approved by our board of directors because, for 2016, no individual objectives were adopted, so awards for all executives were to be based entirely on achievement of the corporate objectives. The incentive targets were 50% of base salary for our Chief Executive Officer and 35% of base salary for the other NEOs. The compensation committee and our board of directors determined that the corporate objectives would align the interests of our executive officers with those of our stockholders and, because awards were to be based entirely on achievement of the corporate objectives, the interests of all our executive officers would be aligned with one another and further promote collaborative effort toward the achievement of the corporate objectives. Under the 2016 Executive Incentive Plan, our board of directors had discretion to grant an award that was less than the incentive target if it determined performance partially met objectives or was less than acceptable, and to grant an incentive award that exceeded the incentive target if it determined performance exceeded objectives or was excellent in view of prevailing conditions; provided that no award could exceed three times a participant's base salary.

Due to the nature and life cycle stage of our business, the corporate objectives under the 2016 Executive Incentive Plan, which were established by our board of directors in March 2016 at the time the 2016 Executive Incentive Plan was adopted, were weighted heavily on advancing our product candidates toward regulatory approval, most heavily with regard to our then-lead product candidate, vepoloxamer, in the U.S. for the treatment of sickle cell crisis. Our board of directors believed timely execution on the Phase 3 clinical study of vepoloxamer and specific progress toward FDA approval of vepoloxamer for the treatment of sickle cell crisis were critical to value creation for our stockholders and, accordingly, set 2016 goals intended to focus the management team in that regard. The 2016 goals

and the relative weighting assigned to each goal were as noted in the table below.

Goal	Weighting
Unblinding of Phase 3 clinical study by June 30th	20 %
Progress toward 2017 submission of New Drug Application for vepoloxamer (assuming Phase 3 study success) or execution on contingency plans (in event of negative Phase 3 results)	40 %
Initiation of 100-patient, investigator-sponsored Phase 2 study of AIR001; enrollment in Phase 2 study of vepoloxamer in heart failure	5 %
Capital funding and cash management consistent with forecast and strategic plans	20 %
Shareholder return relative to peer group	15 %

In January 2017, the compensation committee reviewed performance against the 2016 corporate goals. In light of the delayed timing of unblinding of the Phase 3 clinical study data, the study's failure to achieve its primary efficacy endpoint, and our subsequent decision to discontinue all clinical development of vepoloxamer, the compensation committee determined that key goals were not achieved. However, in reviewing performance, the compensation committee considered the executive officers' accomplishments with respect to executing on our contingency plans in the case of negative Phase 3 study results, including the negotiation and execution of the merger agreement with Savara, as well as successes in advancing the development of AIR001. Ultimately, the compensation committee determined to recommend that no bonuses be awarded under the 2016 Executive Incentive Plan and our board of directors

agreed with that recommendation. Accordingly, the NEOs did not receive any incentive awards under the 2016 Executive Incentive Plan. The following table sets forth the incentive targets and actual payout under the 2016 Executive Incentive Plan:

	Incentive Target		Award Paid	
	(% of base salary)		(% of base salary)	
Named Executive Officer	50	%	0	%
Chief Executive Officer	50	%	0	%
All Other NEOs	35	%	0	%

Long-Term Incentive Awards – Stock Options

We typically grant stock option awards to our employees, including our executive officers, with multi-year, time-based vesting. In 2016, 2015 and 2014, stock option awards were the only equity awards granted to our employees, including the NEOs. All option awards were granted under our stockholder-approved plans that do not permit repricing or exercise prices below the closing sale price of our common stock on the NYSE MKT on the grant date. Stock options granted to employees who have been employed by us for more than one year as of the grant date generally vest on a monthly basis over a four-year period after the grant date. Stock options granted to new employees generally vest monthly over four years after a one-year anniversary “cliff” vesting of 25% of the shares subject to the option. All option awards typically have a 10-year term.

Because vesting occurs over multiple years and only if the employee continues to be employed with us at the time of vesting and because a stock option becomes valuable only if our stock price is greater at the time an option is exercised than it was at the time the option was granted, our board of directors believes these equity awards encourage our employees to remain with our company, promote a long-term perspective on corporate success, directly incentivize the NEOs to build long-term value, and align the interests of our employees, including the NEOs, with our stockholders. The multi-year vesting feature and 10-year term also foster employee retention.

In determining the size of option awards to be granted to our employees, including the NEOs, in 2016, our compensation committee and our board considered, among other things, comparative industry data provided by Barney & Barney, our outstanding shares of and securities exercisable for our common stock, the amount of option awards granted to the NEO in prior years and the retentive value of his/her outstanding option awards, the amount of shares available under our 2015 Omnibus Incentive Plan and desirable run rate and aggregate estimated equity usage in the future, each NEO’s ownership in our company, our corporate performance and each NEOs individual role, responsibilities and performance. The compensation committee and, ultimately, our board of directors exercise discretion in determining the information they consider, as well as the weighting of particular information, in determining the stock option awards. The determination of equity awards is made by our board, taking into account its compensation committee’s recommendations, after evaluating the information and areas of consideration described above in their totality. The option awards to the NEOs for 2016 were approved by our board of directors on December 22, 2015 for grant on the first business day of 2016, which was January 4, 2016, with an exercise price equal to the closing sale price of our common stock on the grant date.

Stock option grant information for 2016 is set forth below under “Grants of Plan-Based Awards.”

Other Elements of Compensation

We maintain broad-based benefits that are provided to all regular, full-time employees (including the NEOs), including health, dental and vision insurance, life and disability insurance, paid time off, and a 401(k) plan. We believe these benefits enable us to offer more competitive compensation packages and support employee focus and productivity.

401(k) Plan and Company Match. We have a defined contribution savings plan pursuant to Section 401(k) of the Internal Revenue Code of 1986. The plan is for the benefit of all employees and permits voluntary contributions by qualifying employees of up to 100% of eligible compensation, subject to Internal Revenue Service-imposed maximum limits. Under the terms of the plan, in 2016, 2015 and 2014, we were required to make matching contributions equal to 100% of employee contributions up to 6% of eligible compensation, limited by the IRS-imposed maximum, for all employees.

Life Insurance Policies. We provide all regular, full-time employees, including the NEOs, with a life insurance policy equal to two times the employee's annual base salary, up to a maximum coverage of \$750,000.

Vacation Time Benefits. Mr. Culley, Ms. Roberts, Dr. Parsley and Ms. Hood accrue 31, 25, 22 and 26 vacation days per year, respectively, subject to annual adjustment based on the number of years of the officer's employment with us. Prior to the conclusion of their full-time employment with us, Dr. Emanuele and Mr. Gorgas both accrued 25 vacation days per year. Under our policy, the maximum number of vacation days that an employee, including the NEOs, can accrue is two times the employee's annual accrual limit. Accrued but unused vacation time is paid upon termination of employment. The amounts paid to Dr. Emanuele and Mr.

Gorgas upon termination of their employment in October 2016 and December 2016, respectively, are set forth in the Summary Compensation Table below. As a temporary, part-time employee, Dr. Emanuele does not accrue vacation time.

Perquisites. We did not provide any of the NEOs with perquisites in 2016 that exceeded \$10,000 in the aggregate for any person.

Executive Severance Agreements

The employment of each of the NEOs is at-will and they or we may terminate their employment with us at any time with or without prior notice, subject to payment of severance benefits under certain circumstances as described below. In March 2016, the compensation committee recommended, and our board of directors approved, an executive severance agreement with each of the NEOs that provides for the severance benefits described below under “Executive Severance Agreements” upon a qualifying termination of employment and the NEO’s compliance with certain post-termination obligations, including delivery of a general release of claims in favor of our company. The March 2016 executive severance agreements replaced and superseded all pre-existing severance arrangements between our company and the NEOs.

In connection with its review of executive compensation for 2016, the compensation committee, with input from Barney & Barney, evaluated existing severance arrangements with our executive officers with a goal of ensuring they serve as an adequate tool for retaining key talent, particularly during volatile and/or transitional periods for our company and considered, among multiple factors, peer company practice and consistency of severance compensation among the executive officers. The compensation committee also specifically considered that, in 2016, we anticipated a pivotal event for our company—the completion of enrollment in and announcement of results of a double-blinded Phase 3 clinical study of our lead product candidate, which, whether positive or negative, could result in new strategic opportunities for our company, and the compensation committee and our board of directors determined it was important to establish severance arrangements that would allow the executive officers to assess strategic opportunities objectively, from the perspective of what is in the best interest of our stockholders, without regard to the potential impact of a transaction on their own job security or personal financial interests. Prior to the 2016 executive severance agreements, the NEOs had disparate severance arrangements that were established in 2009, 2011, 2012 and 2014. Following its review of existing severance arrangements, the compensation committee determined to replace and supersede all existing severance arrangements with an agreement that was consistent among the executive officers, except as to the amount of potential severance benefits, which is greater for our Chief Executive Officer than the other NEOs, as described below under “Potential Payments upon Termination or Change in Control – Executive Severance Agreements.” The compensation committee and our board of directors recognize the potentially significant cost of the severance offered by the executive severance agreements, but believe it is outweighed by value they provide as discussed above and balanced by other factors, such as:

- ❖ No “single trigger” benefits— no severance benefits are triggered solely as a result of a change in control of our company; the executive officer must be involuntarily terminated or resign for good reason to become eligible for severance;
- ❖ No tax gross-up payments are provided for “golden parachute” excise taxes; and
- ❖ Receipt of severance benefits is, in all cases, conditioned upon our receipt of a general release of claims from the NEO in favor of our company that becomes effective.

Factors for Determining 2016 Compensation

Performance

One of the primary objectives of our executive compensation program is to motivate our executive officers to achieve strategic goals that our board of directors believes will lead to short-term and long-term value creation for our

stockholders. As discussed above, given the nature of our business and our life-cycle stage, these goals are largely tied to advancement of our product pipeline through the attainment of clinical and regulatory milestones, securing adequate funding, and managing our cash resources consistent with forecast and strategic plans. Although our annual executive incentive plans establish pre-approved goals, our board of directors retains significant discretion to assess performance in a subjective, non-formulaic manner. This is evidenced by the board's decision not to award any bonuses under the 2016 Executive Incentive Plan, but to provide incentive for continuing efforts leading to consummation of the proposed merger with Savara by establishing the 2017 bonus opportunity for the NEOs described below under "2017 Executive Compensation."

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Peer Group and Competitive Assessment

Our compensation committee believes that establishing a peer group and reviewing compensation packages offered and paid to similar positions of that peer group provides useful information in evaluating our executive compensation practices, including the structure and levels of compensation that will allow us to attract, retain and motivate our executive officers and also align their interests with those of our stockholders. Accordingly, in consultation with Barney & Barney, in the fourth quarter of 2015, the compensation committee established a peer group for a market assessment of our executive compensation ahead of making its recommendations for 2016 executive compensation. Peer companies were identified based on several characteristics, including being publicly traded, industry sector, size (in reference to each of market capitalization, revenues, and number of employees), stage of development of the company's lead drug, and geographic location. The peer group consisted of the following 25 life science companies with an emphasis on specialty pharmaceutical and/or biological products:

AcelRx Pharmaceuticals	CytRx	Neuralstem
Apricus Biosciences	Endocyte	OncoSec Medical
ArQule	Evoke Pharma	Pain Therapeutics
Catabasis Pharmaceuticals	Fate Therapeutics	Palatin Technologies
CEL-SCIC	Glycomimetics	Repros Therapeutics
ChemoCentryx	GTx	Sunesis Pharmaceuticals
Cidara Therapeutics	ImmunoCellular Therapeutics	TRACON Pharmaceuticals
Conatus Pharmaceuticals	MEI Pharma	
Cytokinetics	Mirati Therapeutics	

The executive employment market in our industry in Southern California is competitive because there are many biopharmaceutical, biotechnology, specialty pharmaceutical, and medical device companies in our region that are similar to us in size and stage of development. To effectively recruit, retain and motivate key employees, we believe our executive compensation must be competitive within the peer group and region in which we compete, while also aligned with the interest of our stockholders. The review conducted against similar positions in the peer group established by our compensation committee indicated that actual total direct compensation levels for the NEOs, excluding our General Counsel, were aligned with the median. The General Counsel position was not reviewed because, at the time the compensation committee conducted its assessment, we did not have that position. The assessment also indicated that while total potential ownership levels were above the median, because a large majority of the stock options held by the NEOs were underwater (i.e., the exercise price was above the market price of our common stock), the equity compensation was not serving as a significant incentive for executive retention. The information resulting from this market assessment was a factor in the compensation committee's recommendations for executive compensation for 2016 discussed above; in particular, with respect to recommending the size of stock option awards to be granted in 2016.

Results of "Say on Pay" Advisory Vote on Executive Compensation

At our 2016 annual meeting of stockholders, approximately 77% of shares voted on the "say on pay" proposal approved, on an advisory basis, the compensation paid to our named executive officers as disclosed in our definitive proxy statement for that meeting. The 2016 annual meeting was held on June 15, 2016, by which time our compensation committee had completed its review and recommendations, and our board of directors had approved, executive compensation for 2016. However, the compensation committee does monitor the results of these advisory votes and considers such results in making its executive compensation recommendations to our board of directors. Our

stockholder advisory votes on executive compensation are held every three years. At our 2013 annual meeting of stockholders, approximately 86% of shares voted on the proposal approved, on an advisory basis, the compensation paid to our named executive officers as disclosed in our definitive proxy statement for that meeting. Our executive compensation philosophy, objectives and basic structure remained consistent between the 2013 annual meeting of stockholders and our board's determination of 2016 executive compensation.

2017 Executive Compensation

In determining executive compensation for 2017, the compensation committee considered the results of the Phase 3 clinical study of vepoloxamer and the subsequent negotiation and execution of our merger agreement with Savara on January 6, 2017, taking into account that, if the transactions contemplated by the merger agreement are consummated, they will result in a change in control of our company. On January 17, 2017, the compensation committee recommended and our board of directors made the compensation-related decisions described below in furtherance of retaining, rewarding and incentivizing our remaining executive officers' continuing efforts to help our company achieve its goals through the proposed merger (including consummation of the merger) and to obtain agreement and clarity regarding the effect of the change in control on outstanding stock options held by our current employees and directors. Our board of directors' January 2017 decisions included that there would be no base salary increases for 2017 or awards under the 2016 Executive Incentive Plan (as described above).

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2017 Retention/Performance Bonus

To reward the NEOs for their contributions in negotiating the merger agreement with Savara and incentivize them to continue employment until we consummate the proposed merger in order to continue to operate our business and help ensure the conditions to Savara's obligation to complete the merger are satisfied and the closing occurs as expeditiously as possible, the compensation committee recommended and our board of directors approved a retention/performance bonus payable 50% in a single sum cash payment and 50% in a grant of restricted stock units (RSUs) for the NEOs currently serving as executive officers, with payment of the cash award and vesting of the RSUs contingent upon consummation of the proposed merger on or before July 6, 2017, the NEO's continued service with us until that event, and the NEO's delivery of a general release of claims in our favor. The amounts of these awards are as set forth in the table below:

Named Executive Officer	Cash	RSU
	Award	Award
	(\$)	(# of units)
Brian Culley	53,575	382,679
Brandi Roberts	27,300	195,000
Edwin Parsley	31,900	227,859
Shana Hood	24,500	175,000

The RSUs were granted under our stockholder-approved 2015 Omnibus Incentive Plan. Each RSU represents a right to receive one share of our common stock. The number of RSUs granted to each NEO is the quotient of the amount of the cash award for the NEO divided by the closing sales price of our common stock on the date our board approved these awards, which was \$0.14 per share.

Restricted Stock Units Awards

To further incentivize the NEOs to continue efforts to help our company achieve its goals through the proposed merger with Savara, as well as to reduce our fully-diluted share count and maximize the exchange ratio set forth in the merger agreement for the benefit of our stockholders, the compensation committee determined it would be in the best interests of our company and stockholders to reach an agreement and understanding with the NEOs that all of their outstanding and unexercised stock options would be cancelled immediately prior to, but contingent upon, the consummation of the merger, without any accelerated vesting to which they otherwise may be entitled. Accordingly, upon recommendation of the compensation committee, our board of directors approved RSU awards to the NEOs currently serving as executive officers. In accordance with the notices of grant and agreements governing these awards, the RSUs were granted under our 2015 Omnibus Incentive Plan and will vest in full if the NEO is providing services to us on the date the proposed merger is consummated (provided such date occurs on or before July 6, 2017) or immediately prior to such date. In addition, in accordance with the notices of grant and agreements governing the RSUs, all of the NEOs' outstanding and unexercised stock options will be cancelled immediately prior to, but contingent upon, the consummation of the merger and cease to be exercisable as of such date without any accelerated vesting. Please see below under "Outstanding Equity Awards at Fiscal Year-End 2016" for the number of shares underlying outstanding stock options held by the NEOs as of December 31, 2016. The amounts of these RSU awards to the NEOs are set forth in the table below:

	RSU Award
Named Executive Officer	(# of units)
Brian Culley	1,985,515
Brandi Roberts	694,926
Edwin Parsley	666,713
Shana Hood	278,556

Prohibition on Hedging the Economic Risk of Ownership in Our Securities

As part of our insider trading policy, our directors and employees (including the NEOs) and designated consultants, advisors and contractors to our company are prohibited from engaging in speculative transactions involving our securities, including short sales, “sales against the box” or any equivalent transaction involving our securities (or the securities of any of our customers, vendors, suppliers or other business partners). In addition, as part of our insider trading policy, our directors, executive officers and other specified employees of and consultants, advisors and contractors to our company are prohibited from engaging in hedging or derivative transactions involving our securities, such as “cashless” collars, forward sales, equity swaps and other similar or related transactions, and all other employees and persons subject to the policy are discouraged from engaging in such transactions and required to pre-clear any such proposed transaction with the compliance officer for our insider trading policy. Further, our insider trading policy states that we recommend that our directors and employees (including our executive officers) and other persons subject to the policy not hypothecate or pledge our securities to secure a loan and that they not purchase our securities “on margin” (that is,

borrow funds to purchase securities, including in connection with exercising any stock options), and requires that our directors, officers and other specified employees of and consultants, advisors and contractors to our company pre-clear any proposed margin transaction involving our securities with the compliance officer for our insider trading policy.

Compensation Risk Assessment

The compensation committee's responsibilities include evaluating our executive compensation program to confirm that it does not incentivize excessive risk-taking. Our executive compensation program includes a mix of different types of compensation (base salary, annual performance-based cash bonuses, and long-term equity incentive awards), which provides balance between fixed and performance-based compensation and as to the timing of pay realization. We also believe that our compensation program encourages and rewards prudent business judgment and incentivizes executive officers to achieve near-term goals but not to the detriment of long-term value creation, which further aligns the interests of the executive officers with those of our stockholders. Based on its latest review, the compensation committee concluded that our executive compensation program does not create risks that are reasonably likely to have a material adverse impact on our company.

Conclusion

Attracting, retaining and motivating key employees is essential to creating stockholder value. Offering a competitive compensation program with the right mix of base salary and performance-based compensation, including a substantial equity component, and providing for post-termination compensation in certain circumstances, helps us achieve our business objectives and aligns the interest of our executive officers with those of our stockholders. We believe that our 2016 executive compensation was appropriate in that regard.

Compensation Committee Interlocks and Insider Participation

During 2016, the compensation committee consisted of Dr. Dittrich, Mr. Greenleaf and Mr. Pauls. No member of the compensation committee has ever been an officer or employee of ours. None of our executive officers currently serves, or served during 2016, on the compensation committee or board of directors of any other entity that has one or more executive officers serving as a member of our board of directors or compensation committee.

Compensation Committee Report

The compensation committee of the board of directors of Mast Therapeutics, Inc. has reviewed and discussed with management the Compensation Discussion and Analysis contained in this Annual Report on Form 10-K and, based on such review and discussions, has recommended to the board of directors that the Compensation Discussion and Analysis be included in this Annual Report on Form 10-K.

Submitted by the compensation committee of the board of directors of Mast Therapeutics, Inc.

Howard C. Dittrich
Peter Greenleaf
Matthew Pauls

The material in the foregoing Compensation Committee Report is not "soliciting material," shall not be deemed "filed" with the SEC, and shall not be incorporated by reference in any filing of the Company under the Securities Act of 1933, as amended, the Securities Exchange Act of 1934, as amended, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

Summary Compensation Table

The following table sets forth compensation information for the NEOs for the years ended December 31, 2016, 2015 and 2014:

Name and Principal Position	Year	Summary Compensation Table					Total (\$)
		Salary (\$)	Option Awards (\$)		Incentive Plan Compensation (\$)	All Other Compensation (\$)	
			(1)	(2)			
Brian M. Culley (5) Chief Executive Officer	2016	428,600	359,172	—	17,160	804,932	
	2015	419,175	1,286,155	171,862	17,490	1,894,682	
	2014	405,000	863,039	189,591	16,440	1,474,070	
Brandi L. Roberts (6) Chief Financial Officer & Senior Vice President	2016	312,000	167,629	—	16,589	496,218	
	2015	300,000	494,418	73,800	17,310	885,528	
Edwin L. Parsley (7) Chief Medical Officer & Senior Vice President	2016	364,575	167,629	—	19,409	551,613	
	2015	353,100	637,327	101,340	65,916	(8) 1,157,683	
Shana Hood (9) General Counsel, Vice President & Secretary	2016	280,000	119,714	—	16,512	416,226	
R. Martin Emanuele (10) Former Senior Vice President, Development	2016	266,807	180,413	(11) —	337,034	(12) 784,254	
	2015	310,500	336,172	76,383	21,172	744,227	
	2014	300,000	201,033	84,263	20,078	605,374	
Gregory D. Gorgas (13) Former Senior Vice President, Commercial	2016	297,812	235,430	(14) —	322,548	(15) 855,790	

(1) Amounts shown in this column do not reflect compensation actually received by the NEO. The amounts in this column represent the aggregate grant date fair value of option awards granted to the NEO in the year indicated, calculated in accordance with the provisions of Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 718, Stock Compensation, except that any estimate of forfeitures was disregarded. For a description of the assumptions used to calculate these amounts, see Note 11 to our audited consolidated financial statements included in this annual report.

(2) To the extent not exercised prior to consummation of our proposed merger with Savara, pursuant to the terms of the RSUs described above under “Compensation Discussion and Analysis – 2017 Executive Compensation,” the outstanding stock options held by Mr. Culley, Ms. Roberts, Dr. Parsley and Ms. Hood will be cancelled immediately prior to, and contingent upon, consummation of the merger. All of the outstanding stock options held by the NEOs are underwater (i.e., their exercise price is greater than the market price of our common stock).

Unless the market price of our common stock increases above the applicable exercise price before consummation of the proposed merger, we do not expect these NEOs to exercise any of their outstanding stock options before they are cancelled immediately prior to consummation of the merger and, therefore, the NEOs will derive no value from their stock options.

- (3) We paid the amounts set forth in this column pursuant to the terms of our 2015 Executive Incentive Plan and 2014 Executive Incentive Plan, as applicable. No awards were made under our 2016 Executive Incentive Plan, as described above under “Compensation Discussion and Analysis.”
- (4) Unless otherwise noted, the amounts in this column consist of (a) employer 401(k) plan matching contributions and (b) premiums paid for life insurance policies for the benefit of the NEO.
- (5) Mr. Culley also serves as a member of our board of directors, but he does not receive any additional compensation for such service.
- (6) Ms. Roberts was not an NEO for the year ended December 31, 2014. Accordingly, this table does not include 2014 compensation information for Ms. Roberts.

- (7) Dr. Parsley was not an NEO for the year ended December 31, 2014. Accordingly, this table does not include 2014 compensation information for Dr. Parsley.
- (8) Includes \$45,853 of relocation expense reimbursement and \$2,350 of commuting expense reimbursement prior to Dr. Parsley's relocation to San Diego, all paid pursuant to the terms of Dr. Parsley's employment offer letter, dated September 29, 2014, and in connection with commencement of his employment in October 2014.
- (9) Ms. Hood was not an NEO for the years ended December 31, 2015 or 2014. Accordingly, this table does not include 2015 or 2014 compensation information for Ms. Hood.
- (10) Dr. Emanuele's employment with us terminated on October 28, 2016. He subsequently was re-hired as a temporary, part-time employee to provide transition services, but his service as an executive officer ended on October 28, 2016. As a part-time employee, he is not entitled to any benefits other than legally mandated sick leave and eligibility to participate in our 401(K) plan. Of his total 2016 salary set forth in this table, the amount earned by Dr. Emanuele for his part-time employment was \$4,351.
- (11) This amount represents (a) \$167,629 in aggregate grant date fair value of the option award granted to Dr. Emanuele in January 2016, calculated as described in footnote (1) of this table, and (b) \$12,784 of incremental fair value related to the accelerated vesting applied to all of Dr. Emanuele's outstanding stock options and the post-termination exercised period extension applied to the vested portions (after taking into account the accelerated vesting), in accordance with his Executive Severance Agreement.
- (12) Includes severance of \$256,103 and \$61,204 for accrued but unused vacation time paid in connection with termination of employment pursuant to the terms of Dr. Emanuele's Executive Severance Agreement.
- (13) Mr. Gorgas' employment with us terminated on December 28, 2016. Mr. Gorgas was not an NEO for the years ended December 31, 2015 or 2014. Accordingly, this table does not include 2015 or 2014 compensation information for Mr. Gorgas.
- (14) This amount represents (a) \$167,629 in aggregate grant date fair value of the option award granted to Mr. Gorgas in January 2016, calculated as described in footnote (1) of this table, and (b) \$67,801 of incremental fair value related to the accelerated vesting applied to all of Mr. Gorgas's outstanding stock options and the post-termination exercised period extension applied to the vested portions (after taking into account the accelerated vesting), in accordance with his Executive Severance Agreement.
- (15) Includes severance of \$249,277 and \$55,850 for accrued but unused vacation time paid in connection with termination of employment pursuant to the terms of Mr. Gorgas's Executive Severance Agreement.

Grants of Plan-Based Awards

The following table sets forth information regarding grants of plan-based awards to the NEOs for the year ended December 31, 2016:

Grants of Plan-Based Awards in Fiscal Year 2016									
Name	Type of Award (1)	Grant Date (2)	Board Approval Date	Estimated Possible Payouts Under Threshold (\$)	Non-Equity Incentive Plan Award Maximum (\$)	Option Awards: Number of Securities Underlying Options (#)	Exercise Price (\$/Sh)	Grant Date	Fair Value of Option Awards (\$)
Brian M. Culley	AIP	—	—	—	214,300	—	—	—	—
	SO	01/04/2016	01/04/2016	—	—	1,227,100	0.42	—	359,172
Brandi L. Roberts	AIP	—	—	—	109,200	—	—	—	—
	SO	01/04/2016	01/04/2016	—	—	572,700	0.42	—	167,629
Edwin L. Parsley	AIP	—	—	—	127,601	—	—	—	—
	SO	01/04/2016	01/04/2016	—	—	572,700	0.42	—	167,629
Shana Hood	AIP	—	—	—	98,000	—	—	—	—
	SO	01/04/2016	01/04/2016	—	—	409,000	0.42	—	119,714
R. Martin Emanuele	AIP	—	—	—	111,391	—	—	—	—
	SO	01/04/2016	01/04/2016	—	—	572,700	0.42	—	180,413 (6)
Gregory D. Gorgas	AIP	—	—	—	105,098	—	—	—	—
	SO	01/04/2016	01/04/2016	—	—	572,700	0.42	—	235,430 (7)

(1) Type of Award:
AIP: Annual Incentive Plan

SO: Stock Option

(2) These stock option awards were approved for grant on the first day of 2016 on which the markets were open, which day was January 4, 2016.

(3) Amounts shown in these columns represent the possible award amounts under the 2016 Executive Incentive Plan. No awards were actually made under this plan, as reflected in the Summary Compensation Table in the “Non-Equity Incentive Plan Compensation” column and discussed above under “Compensation Discussion and Analysis.” There were no threshold amounts established under the 2016 Executive Incentive Plan. Actual payout amounts were subject to the discretion of our board of directors could range from zero to three times an executive’s base salary.

- (4) In accordance with the terms of our 2015 Omnibus Incentive Plan, under which these stock option awards were granted, the exercise price of each option was set at the closing market price of our common stock on the grant date.
- (5) For a description of the assumptions used to calculate the grant date fair value of these option awards, see Note 11 to our audited consolidated financial statements included in this annual report. However, the amounts in this column do not reflect estimated forfeitures.
- (6) This amount represents (a) \$167,629 in aggregate grant date fair value of the option award granted to Dr. Emanuele in January 2016, calculated as described in footnote (5) of this table, and (b) \$12,784 of incremental fair value related to the accelerated vesting applied to all of Dr. Emanuele's outstanding stock options and the post-termination exercised period extension applied to the vested portions (after taking into account the accelerated vesting), in accordance with his Executive Severance Agreement.
- (7) This amount represents (a) \$167,629 in aggregate grant date fair value of the option award granted to Mr. Gorgas in January 2016, calculated as described in footnote (5) of this table, and (b) \$67,801 of incremental fair value related to the accelerated vesting applied to all of Mr. Gorgas's outstanding stock options and the post-termination exercised period extension applied to the vested portions (after taking into account the accelerated vesting), in accordance with his Executive Severance Agreement.

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Outstanding Equity Awards at Fiscal Year-End 2016

The following table sets forth information regarding outstanding equity awards held by the NEOs as of December 31, 2016. Share and per share information included in this table for option awards granted before April 23, 2010 reflects retrospective application of the 1-for-25 reverse split of our outstanding common stock effected on April 23, 2010.

Name	Option Awards		Price	Option
	Number of Securities Underlying Unexercised Options (#)	Number of Securities Underlying Unexercised Options (#)		
Brian M. Culley (2)	Exercisable(1)	Unexercisable(1)	(\$/Sh)	Expiration Date
	5,999	—	68.75	01/11/2017
	8,000	—	13.50	03/30/2018
	67,999	—	3.25	07/20/2019
	63,999	—	8.00	02/02/2020
	100,000	—	2.29	02/01/2021
	250,000	—	3.26	07/05/2021
	425,000	—	0.60	12/07/2021
	135,761 (3)	2,889	(3) 0.59	01/02/2023
	793,887 (4)	113,413	(4) 0.50	06/19/2023
	474,177 (5)	176,123	(5) 0.47	01/02/2024
	696,406 (6)	417,844	(6) 0.65	06/19/2024
Brandi L. Roberts (2)	1,006,513 (7)	1,094,037	(7) 0.58	01/02/2025
	333,337 (8)	555,563	(8) 0.50	06/11/2025
	281,210 (12)	945,890	(12) 0.42	01/04/2026
	85,000	—	2.35	06/04/2021
	140,000	—	0.60	12/07/2021
	74,171 (3)	1,579	(3) 0.59	01/02/2023
	263,593 (4)	37,657	(4) 0.50	06/19/2023
	73,791 (5)	27,409	(5) 0.47	01/02/2024
Edwin L. Parsley (2)	210,375 (6)	126,225	(6) 0.65	06/19/2024
	346,341 (7)	376,459	(7) 0.58	01/02/2025
	166,650 (8)	277,750	(8) 0.50	06/11/2025
	131,243 (12)	441,457	(12) 0.42	01/04/2026
	325,000 (9)	275,000	(9) 0.59	06/19/2024
	384,442 (10)	553,858	(10) 0.58	01/02/2025
	186,730 (11)	369,120	(11) 0.50	06/11/2025
131,243 (12)	441,457	(12) 0.42	01/04/2026	

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Shana Hood (2)	11,250	—	5.91	03/16/2020
	27,069	—	2.29	02/01/2021
	37,450	—	0.60	12/07/2021
	21,933	(3) 467	(3) 0.59	01/02/2023
	83,562	(4) 11,938	(4) 0.50	06/19/2023
	18,666	(5) 6,934	(5) 0.47	01/02/2024
	58,531	(6) 35,119	(6) 0.65	06/19/2024
	84,572	(7) 91,928	(7) 0.58	01/02/2025
	80,925	(8) 134,875	(8) 0.50	06/11/2025
93,729	(12) 315,271	(12) 0.42	01/04/2026	
R. Martin Emanuele (13)	101,413	—	0.47	07/31/2017
	219,996	—	0.65	07/31/2017
	312,656	—	0.58	07/31/2017
	151,823	—	0.50	07/31/2017
	214,761	—	0.42	07/31/2017

Gregory D. Gorgas (13)	100,000	—3.44	09/30/2017
	160,000	—0.60	09/30/2017
	58,250	—0.59	09/30/2017
	292,096	—0.50	09/30/2017
	43,248	—0.47	09/30/2017
	241,736	—0.65	09/30/2017
	415,201	—0.58	09/30/2017
	234,619	—0.50	09/30/2017
	238,625	—0.42	09/30/2017

- (1) The vesting schedules described for each option in this table are subject to the NEO’s continued service to our company and to acceleration in connection with an involuntary termination, as described below under “Potential Payments upon Termination or Change in Control - Executive Severance Agreements.”
- (2) To the extent not exercised prior to consummation of our proposed merger with Savara, pursuant to the terms of the RSUs described above under “Compensation Discussion and Analysis – 2017 Executive Compensation,” the outstanding stock options held by Mr. Culley, Ms. Roberts, Dr. Parsley and Ms. Hood will be cancelled immediately prior to, and contingent upon, consummation of the merger. All of the outstanding stock options held by the NEOs are underwater (i.e., their exercise price is greater than the market price of our common stock). Unless the market price of our common stock increases above the applicable exercise price before consummation of the proposed merger, we do not expect these NEOs to exercise any of their outstanding stock options before they are cancelled immediately prior to consummation of the merger and, therefore, we expect all of their outstanding stock options will be cancelled as of the date of consummation of the proposed merger.
- (3) This option vests and becomes exercisable in substantially equal monthly installments over four years. Approximately 1/48th of the total underlying shares vested and became exercisable on February 2, 2013 and will vest and become exercisable on the second day of each month thereafter.
- (4) This option vests and becomes exercisable in substantially equal monthly installments over four years. Approximately 1/48th of the total underlying shares vested and became exercisable on July 19, 2013 and will vest and become exercisable on the nineteenth day of each month thereafter.
- (5) This option vests and becomes exercisable in substantially equal monthly installments over four years. Approximately 1/48th of the total underlying shares vested and became exercisable on February 2, 2014 and will vest and become exercisable on the second day of each month thereafter.
- (6) This vests and becomes exercisable in substantially equal monthly installments over four years. Approximately 1/48th of the total underlying shares vested and became exercisable on July 19, 2014 and will vest and become exercisable on the nineteenth day of each month thereafter.
- (7) This vests and becomes exercisable in substantially equal monthly installments over four years. Approximately 1/48th of the total underlying shares vested and became exercisable on July 19, 2014 and will vest and become

exercisable on the nineteenth day of each month thereafter.

- (8) This option vests and becomes exercisable in substantially equal monthly installments over four years. Approximately 1/48th of the total underlying shares vested and became exercisable on July 11, 2015 and will vest and become exercisable on the eleventh day of each month thereafter.
- (9) This option vests and becomes exercisable in substantially equal monthly installments over three years after a one-year “cliff” vesting. Approximately 1/4 of the total underlying shares vested and became exercisable on October 1, 2015 and approximately 1/36th of the balance of the underlying shares will vest and become exercisable on the first day of each of the 36 months thereafter.
- (10) This option vests and becomes exercisable in substantially equal monthly installments over four years after a “cliff” vesting on the first anniversary of Dr. Parsley’s employment start date. 156,383 of the underlying shares vested and became exercisable on October 1, 2015 and approximately 1/48th of the balance of the underlying shares vests and becomes exercisable on the first day of each month thereafter.

- (11) This option vests and becomes exercisable in substantially equal monthly installments over four years after a “cliff” vesting on the first anniversary of Dr. Parsley’s employment start date. 34,740 of the underlying shares vested and became exercisable on October 1, 2015 and approximately 1/48th of the balance of the underlying shares vests and becomes exercisable on the first day of each month thereafter.
- (12) This option vests and becomes exercisable in substantially equal monthly installments over four years. Approximately 1/48th of the total underlying shares vested and became exercisable on February 4, 2016 and will vest and become exercisable on the fourth day of each month thereafter.
- (13) In accordance with their Executive Severance Agreements, the portions of Dr. Emanuele’s and Mr. Gorgas’ stock options that were vested as of their respective dates of termination (taking into account the vesting acceleration provided under the Executive Severance Agreement) are exercisable until July 31, 2017 or September 30, 2017, as applicable. To the extent not exercised on or before those dates, the stock options will be cancelled. See below under “Potential Payments upon Termination or Change in Control - Executive Severance Agreements” for discussion of the terms of the Executive Severance Agreements.

Option Exercises and Stock Vested in Fiscal Year 2016

During the year ended December 31, 2016, none of the NEOs exercised stock options and none held any equity awards other than stock options. Therefore, there is no information to report regarding exercise or vesting of equity awards.

Pension Benefits

We do not maintain any plan that provides for payments or other benefits at, following, or in connection with retirement, other than a 401(k) plan.

Nonqualified Deferred Compensation

We do not maintain any defined contribution or other plan that provides for the deferral of compensation on a basis that is not tax-qualified.

Potential Payments upon Termination or Change in Control

Executive Severance Agreements

As discussed above under “Compensation Discussion and Analysis,” in March 2016, we entered into new severance agreements with the NEOs, which replaced and superseded each NEO’s pre-existing severance arrangements with us. The Executive Severance Agreements with the NEOs require us to make specified payments and provide specified benefits related to their outstanding stock option awards in the event of a qualifying termination of employment, subject to the NEO’s compliance with the terms and conditions in the agreement. No payments or other benefits to the NEOs are triggered under the agreements solely by the occurrence of a change in control of our company—all are “double trigger” benefits.

The following table summarizes the severance benefits to the NEOs under the March 2016 executive severance agreements, or the Executive Severance Agreements. To be eligible for these severance benefits, there must be a qualifying termination of the NEO’s employment and the NEO must execute, deliver and not revoke a general release of claims in our favor. If the NEO holds any other positions with our company, he/she must also resign from positions. A qualifying termination is a termination of employment by us without cause or by the NEO for good reason. Termination as a result of an NEO’s death or disability is not a qualifying termination. In the event of a change in control of our company, the NEO is eligible for the severance benefits if the qualifying termination occurs within 24 months of the effective date of the change in control. No tax gross-up payments are provided under the Executive Severance Agreements.

		Benefits upon	Benefits upon
		Qualifying Termination	Qualifying Termination due to
			Change in Control
Officer Chief Executive Officer	Cash	•Lump sum payment equal to 24 months of current base salary	•Lump sum payment equal to 24 months of current base salary
	Benefits	•Lump sum payment equal to premiums for continued health insurance coverage for 24 months	•Lump sum payment equal to premiums for continued health insurance coverage for 24 months
	Equity	•Vesting acceleration of 25% of total option shares •Exercise period extended to end of 12th month after termination date	•Vesting acceleration of 100% of total option shares •Exercise period extended to 10-year anniversary of option grant date
All Other NEOs	Cash	•Lump sum payment equal to 9 months of current base salary	•Lump sum payment equal to 9 months of current base salary
	Benefits	•Lump sum payment equal to premiums for continued health insurance coverage for 9 months	•Lump sum payment equal to premiums for continued health insurance coverage for 9 months
	Equity	•Vesting acceleration of 18.75% of total option shares •Exercise period extended to end of 9th month after termination date	•Vesting acceleration of 100% of total option shares •Exercise period extended to 10-year anniversary of option grant date

Under the Executive Severance Agreements:

“Cause” means (a) any act of personal dishonesty taken by the executive in connection with the executive’s responsibilities as an employee which is intended to result in substantial personal enrichment of the executive; (b) the executive’s conviction of a felony that our board of directors reasonably believes has had or will have a material detrimental effect on the reputation or business of our company or of our affiliates; (c) a willful act by the executive that constitutes misconduct and is materially injurious to our company or to our affiliates; (d) any material breach by the executive of any offer letter or confidential information, non-solicitation or invention assignment agreement or other agreement entered into with us; or (e) continued willful violations by the executive of the executive’s obligations to our company or to our affiliates after there has been delivered to the executive a written demand for performance that describes the basis for our belief that the executive has not substantially performed the executive’s duties.

“Good reason” means, in each case, without the executive’s express written consent, (a) a material reduction or alteration of the executive’s duties, position or responsibilities relative to those in effect immediately prior to such reduction or alteration, or the executive’s removal from such position, duties or responsibilities; (b) a material reduction of the executive’s base salary as in effect immediately prior to such reduction (unless pursuant to a salary reduction program applicable generally to similarly situated employees); or (c) the relocation of the executive’s

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principal place of employment with our company by more than 50 miles. The severance agreements provide us with a 30-day cure period following written notice from an executive of the occurrence of an event that otherwise would constitute good reason and the executive must have provided that notice to us within 90 days of the executive's awareness of the initial existence of the applicable event.

*"Change in control" has the meaning ascribed to it in our 2015 Omnibus Incentive Plan, as may be amended or restated from time to time, or such other equity incentive plan as may be adopted by our board of directors and approved by our stockholders. Generally, under our 2015 Omnibus Incentive Plan, a change in control occurs upon (a) the consummation of a merger or consolidation of our company with or into another entity, (b) the consummation of the sale, transfer or other disposition of all or substantially all of our assets, (c) certain changes in the majority of our board of directors within a period of 36 consecutive months, (d) the acquisition, pursuant to a tender or exchange offer made directly to our stockholders that our board of directors does not recommend, of more than 50% of the total combined voting power in our outstanding securities, or (e) approval by our stockholders of a plan of complete liquidation or dissolution.

Potential Payments Upon a Qualifying Termination of Employment

The following table sets forth quantitative estimates of the benefits that would have accrued to each of the NEOs pursuant to the Executive Severance Agreements and our vacation policy if there had been a qualifying termination of his/her employment on December 31, 2016. However, for Dr. Emanuele and Mr. Gorgas, each of whom had a qualifying termination before December 31, 2016, their actual benefits are set forth in the following table.

Name	Cash Severance Based on Salary	Cash Severance Based on Health Insurance	Value of Accelerated Option Awards	Value of Accrued Vacation Time	Total
Brian M. Culley	857,200	66,746	—	102,205	1,026,151
Brandi L. Roberts	234,000	24,548	—	60,000	318,548
Edwin L. Parsley	273,431	24,548	—	40,019	337,998
Shana Hood	210,000	23,939	—	55,995	289,934
R. Martin Emanuele	238,695	17,408	—	61,204	317,307
Gregory D. Gorgas	225,210	24,067	—	55,850	305,127

(1) Calculated using annual base salary in effect as of December 31, 2016. No base salary changes have been approved for 2017.

(2) Calculated using insurance premiums in effect as of December 31, 2016.

(3) No value is reflected for vesting acceleration of option awards because the closing market price of our common stock on December 30, 2016 (\$0.09 per share) was less than the exercise price per share of the outstanding stock options held by the NEOs. December 31, 2016 was a Saturday; the markets were not open. Under the terms of the

Executive Severance Agreements, the stock options held by the NEOs upon a qualifying termination due to a change in control (taking into account the vesting acceleration) would remain exercisable through the 10-year anniversary of the option's grant date. This exercise period extension benefit is not quantified in this table.

Potential Payments Upon a Qualifying Termination of Employment due to Change in Control

The following table sets forth quantitative estimates of the benefits that would have accrued to each of the NEOs pursuant to the Executive Severance Agreements and our vacation policy if there had been a change in control of our company and qualifying termination of the NEOs' employment on December 31, 2016. Because Dr. Emanuele and Mr. Gorgas each had a qualifying termination before December 31, 2016, they are excluded from the following table. See the table above under "Potential Payments Upon a Qualifying Termination of Employment" for actual benefits they received in connection with termination of their employment.

Name	Cash Severance Based on Salary (\$ (1))	Cash Severance Based on Health Insurance Cost to Continue (\$ (2))	Value of Accelerated Option Awards (\$ (3)(4))	Value of Accrued Vacation Time (\$)	Total (\$ (5))
Brian M. Culley	857,200	66,746	—	102,205	1,026,151
Brandi L. Roberts	234,000	24,548	—	60,000	318,548
Edwin L. Parsley	273,431	24,548	—	40,019	337,998
Shana Hood	210,000	23,939	—	55,995	289,934

(1) Calculated using annual base salary in effect as of December 31, 2016. No base salary changes have been approved for 2017.

(2) Calculated using insurance premiums in effect as of December 31, 2016.

(3) No value is reflected for vesting acceleration of option awards because the closing market price of our common stock on December 30, 2016 (\$0.09 per share) was less than the exercise price per share of the outstanding stock options held by the NEOs. December 31, 2016 was a Saturday; the markets were not open. Under the terms of the Executive Severance Agreements, the stock options held by the NEOs upon a qualifying termination due to a change in control (taking into account the vesting acceleration) would remain exercisable through the 10-year anniversary of the option's grant date. This exercise period extension benefit is not quantified in this table.

(4) To the extent not exercised prior to consummation of our proposed merger with Savara, pursuant to the terms of the RSUs described above under "Compensation Discussion and Analysis – 2017 Executive Compensation," the outstanding stock options held by the NEOs will be cancelled immediately prior to, and contingent upon, consummation of the merger.

(5) The amounts shown in this column assume full payment of severance benefits, without any reduction to which an NEO may agree to avoid an excise tax on any compensation deemed to be an "excess parachute payment" under Section 280G of the Internal Revenue Code.

Director Compensation

The following table shows compensation information for the individuals who served as non-employee directors during the year ended December 31, 2016. Mr. Culley, our only director who is also one of our employees, does not receive any additional compensation for his service as a director.

Director Compensation for Fiscal Year 2016

Name	Fees Earned or Paid in Cash		Option Awards	Total (\$)
	(\$)	(1) (2)	(3)	
Matthew Pauls	76,426	22,672	99,098	
Howard C. Dittrich	57,038	22,672	79,710	
Peter Greenleaf	50,500	22,672	73,172	
David A. Ramsay	60,038	22,672	82,710	
Lewis J. Shuster (4)	17,904	—	17,904	

(1) Amounts in this column do not reflect compensation actually received by the directors. The amounts in this column represent the aggregate grant date fair value of option awards granted to the directors in 2016, calculated in accordance with the provisions of FASB ASC Topic 718, Stock Compensation, except that any estimate of forfeitures was disregarded. For a description of the assumptions used to calculate these amounts, see Note 11 to our audited consolidated financial statements included in this annual report.

(2) To the extent not exercised prior to consummation of our proposed merger with Savara, the outstanding stock options held by the directors will be cancelled immediately prior to, and contingent upon, consummation of the merger. All of the outstanding stock options held by the directors are underwater (i.e., their exercise price is greater than the market price of our common stock). Unless the market price of our common stock increases above the applicable exercise price before consummation of the proposed merger, we do not expect the directors to exercise any of their outstanding stock options before they are cancelled immediately prior to consummation of the merger and, therefore, the directors will derive no value from their stock options.

(3) As of December 31, 2016, our non-employee directors had option awards outstanding to purchase the following number of shares of our common stock:

Name	Shares Underlying
------	----------------------

Outstanding
Options

(#)

Matthew Pauls	182,136
Howard C. Dittrich	255,732
Peter Greenleaf	182,136
David A. Ramsay	319,844
Lewis J. Shuster	214,384

(4) Mr. Shuster resigned from our board effective March 10, 2016.

Overview of Non-Employee Director Compensation

Compensation of the non-employee members of our board of directors for their service on the board and its committees is set forth in a written policy adopted by our board of directors. With the assistance of its compensation committee, our board of directors periodically reviews and evaluates the director compensation policy and adopts changes designed to allow us to recruit and retain individuals with the requisite experience, skills and characteristics for membership on our board of directors. Our current non-employee director compensation policy was adopted by our board of directors in December 2014 and has been in effect since January 1, 2015. The policy provides for a combination of cash compensation in the form of a fixed retainer and equity compensation in the form of stock option awards. We also reimburse our directors for travel and other reasonable out-of-pocket expenses related to attendance at meetings of our board of directors and its committees. Our non-employee directors do not receive meeting attendance fees, except in the case of service on ad hoc or special committees established by the board. Each non-employee director who serves on an on ad hoc or special committee is eligible to receive \$1,000 for each meeting attended whether attendance is in person or by telephone, videoconference or other comparable communication device. During 2016, our board of directors established a pricing

committee consisting of Messrs. Pauls, Culley, Ramsay and Shuster, which met three times, and a strategic transactions committee consisting of Messrs. Pauls, Greenleaf and Ramsay and Dr. Dittrich, which met six times.

Retainer

The following table reflects the amount of the cash retainer payable to each non-employee director under our director compensation policy based on the director's role on our board and its committees. The amounts set forth in the following table are annualized amounts, which we pay in four equal installments on a quarterly basis. A non-employee director whose service begins or ends during a quarter receives a pro-rated portion of the applicable payment.

2016 Cash Retainer

	Chairperson	Member
	(\$)	(\$)
Board of Directors	60,000	35,000
Audit Committee	15,000	7,500
Compensation Committee	10,000	5,000
Nominating and Governance Committee	10,000	5,000

Equity Compensation

Stock Option Awards

Pursuant to our director compensation policy, non-employee directors are eligible, in connection with each annual meeting of our stockholders, to receive an "annual option" to purchase up to such number of shares of our common stock that is equal to the sum of (a) an amount, which we refer to as the "allocated amount," equal to the product of 0.0396% multiplied by the number of shares of our common stock outstanding as of the date of the applicable annual meeting of stockholders and (b) an amount, which we refer to as the "adjustment amount," equal to the difference between (i) the allocated amount for the current year's annual meeting of stockholders, minus (ii) the allocated amount that was applicable to the prior year's annual meeting of stockholders (unless a director was not a non-employee director at the time of the prior year's annual meeting of stockholders, in which case the adjustment amount for that director will be based on the number of shares of our common stock outstanding as of the date of that director's appointment or election to our board of directors). However, the adjustment amount will be included in the annual option for a director only if (x) the adjustment amount for that director exceeds 20% of the allocated amount for the current year's annual meeting of stockholders, (y) our company's market capitalization (shares outstanding multiplied by stock price) has not exceeded \$100 million for a sustained period, as determined unanimously by our board of directors, and (z) our board of directors unanimously determines to include the adjustment amount in such annual option. Each annual option will vest and become exercisable in 12 substantially equal monthly installments of 1/12th of the shares subject to the option at the end of each successive month following the date of the applicable annual meeting of stockholders, subject to the director's continuing services (as defined in the 2015 Omnibus Incentive Plan).

In addition, any newly appointed or elected non-employee director is eligible to receive an "inducement option" and a "pro-rated annual option." An inducement option entitles the director to purchase up to such number of shares of our common stock that is equal to the amount, which we refer to as the "new director allocated amount," that is the product of 0.0396% multiplied by the number of shares of our common stock outstanding as of the date of the director's initial appointment or election to our board of directors. A pro-rated annual option entitles the director to purchase up to such number of shares of our common stock that is equal to the product of (A) the quotient of the new director allocated

amount, divided by 12, and (B) the number of full 30-day periods between the new director's date of appointment or election and the date of our next annual meeting of stockholders (or, if, on the new director's date of appointment or election, the date of our next annual meeting of stockholders has not been set, the one-year anniversary of the new director's date of appointment or election). Each inducement option will vest and become exercisable in 36 substantially equal monthly installments of 1/36th of the shares subject to the option at the end of each successive month following the date of the director's initial appointment or election to our board of directors, subject to the director's continuing services (as defined in the 2015 Omnibus Incentive Plan). Each pro-rated annual option will vest and become exercisable in such number of substantially equal monthly installments as is equal to the number of full 30-day periods between the director's initial appointment or election to our board of directors and the date of the next annual meeting of our stockholders.

Each stock option award granted pursuant to our director compensation policy will be granted under the 2015 Omnibus Incentive Plan, or any amendment or restatement thereof, will have an exercise price per share equal to the fair market value (as defined in the 2015 Omnibus Incentive Plan) of a share of our common stock on the date the option award is granted, and will have a term equal to the shorter of (i) ten years from the date the option award is granted (subject to a 30-day extension in certain limited circumstances) and (ii) three years from the date such non-employee director ceases to provide services (as defined in the 2015 Omnibus Incentive Plan) to us for any reason other than such director's death or disability. In addition, in the event of a

change of control of our company, each option award will vest and become exercisable on the day prior to the date of the change in control if the director is then providing services (as defined in the 2015 Omnibus Incentive Plan), and each option award will terminate on the date of the change in control to the extent not exercised.

Restricted Stock Unit Awards

On January 17, 2017, to reduce our fully-diluted share count and maximize the exchange ratio set forth in our merger agreement with Savara for the benefit of our stockholders and reach an understanding and agreement with our directors that all of their outstanding and unexercised stock options would be cancelled upon consummation of the proposed merger, upon the recommendation of its compensation committee, our board of directors approved a grant of RSUs to each non-employee director under the 2015 Omnibus Incentive Plan in the amounts set forth in the table below. Each RSU represents a right to receive one share of our common stock. The RSUs will vest in full if the director is providing services to our company on the date the proposed merger with Savara is consummated (provided such date occurs on or before July 6, 2017) or immediately prior to such date. In addition, in accordance with the applicable notices of grant and agreements governing these RSUs, all of the outstanding and unexercised stock options held by the directors will be cancelled immediately prior to, but contingent upon, the consummation of the merger and cease to be exercisable as of such date without any accelerated vesting.

	RSU Awards
Name	(# of units)
Matthew Pauls	45,535
Howard C. Dittrich	63,933
Peter Greenleaf	45,535
David A. Ramsay	79,962

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.
Security Ownership of Certain Beneficial Owners and Management

The following table sets forth information regarding beneficial ownership of our common stock as of March 2, 2017 (the "Evaluation Date"), or an earlier date for information based on filings with the SEC, by (a) each person known to us to beneficially own more than 5% of the outstanding shares of our common stock, (b) each director, (c) each of the named executive officers listed in the compensation tables included in this annual report, and (d) all of our current directors and executive officers as a group. The information in this table is based solely on statements in filings with the SEC or other reliable information. Percent of beneficial ownership is based on 254,746,933 shares of our common stock outstanding as of the Evaluation Date.

Name and Address of Beneficial Owner (1)	Shares		
	Owned (2)	Beneficially	Percent of Outstanding
Principal Stockholders:			
Sabby Management, LLC (3) 10 Mountainview Road, Suite 205 Upper Saddle River, NJ 07458	25,449,219	9.08	%
Directors and Named Executive Officers:			
Brian M. Culley (4)	5,247,710	2.02	%
Matthew Pauls (5)	136,481	*	
Howard C. Dittrich (6)	239,883	*	
Peter Greenleaf (7)	134,681	*	
David A. Ramsay (8)	406,585	*	
Brandi L. Roberts (9)	1,737,320	*	
Edwin L. Parsley (10)	1,273,371	*	
Shana Hood (11)	602,824	*	
R. Martin Emanuele (12)	1,295,247	*	
Gregory D. Gorgas (13)	1,783,775	*	
All directors and executive officers as a group (8 persons) (14)	9,778,855	3.70	%

*Less than 1%

(1) Unless otherwise indicated, the address of each of the listed persons is c/o Mast Therapeutics, Inc., 3611 Valley Centre Drive, Suite 500, San Diego, California 92130.

(2) Beneficial ownership of shares is determined in accordance with SEC rules and generally includes any shares over which a person exercises sole or shared voting or investment power, or of which a person has the right to acquire ownership within 60 days of the Evaluation Date. The RSUs granted to our directors and executive officers in

January 2017 are not included in the beneficial ownership amounts in this table because the vesting/settlement of those RSUs is contingent upon the consummation of our proposed merger with Savara. Except as otherwise noted, (a) each person or entity has sole voting and investment power with respect to the shares shown and (b) none of the shares shown as beneficially owned on this table are subject to pledge. In calculating the percentage ownership of each person identified in the table, shares underlying options, warrants or other rights to acquire shares of our common stock held by that person that are either currently exercisable or exercisable within 60 days of the Evaluation Date are deemed outstanding. These shares, however, are not deemed outstanding for the purposes of computing the percentage ownership of any other individual or entity. Percentage ownership for each person is based on the number of shares of our common stock outstanding as of the Evaluation Date, together with the applicable number of shares of common stock subject to options, warrants or other rights to acquire shares of our common stock currently exercisable or exercisable within 60 days of the Evaluation Date for that person or group of persons. The information in this table reflects the proportionate adjustments made to stock options exercisable for our common stock that we issued prior to the 1-for-25 reverse split of our common stock effected on April 23, 2010.

(3) The number of shares listed for Sabby Management, LLC (“Sabby Management”) and the following information in this footnote was obtained from a Schedule 13G jointly filed with the SEC on January 9, 2017 by Sabby Management, Sabby Healthcare Master Fund, Ltd., Sabby Volatility Warrant Master Fund, Ltd, and Hal Mintz, as well as supplemental information provided by Sabby Management to Mast relating to beneficial ownership as of December 31, 2016. All of the shares listed in the table consist of shares subject to outstanding warrants of Mast that are currently exercisable; none represent shares of Mast common stock that are currently outstanding. The warrants include provisions that block the holder from exercising the warrants to the

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extent that delivery of the shares of Mast's common stock would result in such holder (together with such holder's affiliates and any other persons acting as a group together with such holder's affiliates) having a beneficial ownership in excess of 9.99% of Mast's outstanding common stock. Accordingly, Sabby Healthcare Master Fund, Ltd. beneficially owns 23,952,519 shares and Sabby Volatility Warrant Master Fund, Ltd. owns 1,496,700 shares. Sabby Management and Mr. Mintz do not directly own any securities, but each has shared power to vote or to direct the vote and shared power to dispose or to direct the disposition of 25,449,219 shares. Sabby Management is the investment manager of Sabby Healthcare Master Fund, Ltd. and Sabby Volatility Warrant Master Fund, Ltd. and Mr. Mintz is manager of Sabby Management. The address of Sabby Healthcare Master Fund, Ltd. and Sabby Volatility Warrant Master Fund, Ltd. is c/o Ogier Fiduciary Services (Cayman) Limited, 89 Nexus Way, Camana Bay, Grand Cayman KY1-9007, Cayman Islands.

- (4) Consists of (a) 5,213,210 shares of common stock subject to options currently exercisable or exercisable within 60 days of the Evaluation Date and (b) 34,500 shares of common stock held directly by Mr. Culley. In accordance with the notice of grant and agreement governing the RSUs granted to Mr. Culley in January 2017, immediately prior to, but contingent upon, the consummation of the proposed merger with Savara, all outstanding and unexercised stock options held by Mr. Culley will be cancelled and cease to be exercisable as of such time without any accelerated vesting.
- (5) Consists of 136,481 shares of common stock subject to options currently exercisable or exercisable within 60 days of the Evaluation Date. In accordance with the notice of grant and agreement governing the RSUs granted to Mr. Pauls in January 2017, immediately prior to, but contingent upon, the consummation of the proposed merger with Savara, all outstanding and unexercised stock options held by Mr. Pauls will be cancelled and cease to be exercisable as of such time without any accelerated vesting.
- (6) Consists of 239,883 shares of common stock subject to options currently exercisable or exercisable within 60 days of the Evaluation Date. In accordance with the notice of grant and agreement governing the RSUs granted to Dr. Dittrich in January 2017, immediately prior to, but contingent upon, the consummation of the proposed merger with Savara, all outstanding and unexercised stock options held by Dr. Dittrich will be cancelled and cease to be exercisable as of such time without any accelerated vesting.
- (7) Consists of 134,681 shares of common stock subject to options currently exercisable or exercisable within 60 days of the Evaluation Date. In accordance with the notice of grant and agreement governing the RSUs granted to Mr. Greenleaf in January 2017, immediately prior to, but contingent upon, the consummation of the proposed merger with Savara, all outstanding and unexercised stock options held by Mr. Greenleaf will be cancelled and cease to be exercisable as of such time without any accelerated vesting.
- (8) Consists of (a) 306,585 shares of common stock subject to options currently exercisable or exercisable within 60 days of the Evaluation Date and (b) 100,000 shares of common stock held directly by Mr. Ramsay. In accordance with the notice of grant and agreement governing the RSUs granted to Mr. Ramsay in January 2017, immediately prior to, but contingent upon, the consummation of the proposed merger with Savara, all outstanding and unexercised stock options held by Mr. Ramsay will be cancelled and cease to be exercisable as of such time without any accelerated vesting.

- (9) Consists of 1,699,320 shares of common stock subject to options currently exercisable or exercisable within 60 days of the Evaluation Date and (b) 38,000 shares of common stock held directly by Ms. Roberts. In accordance with the notice of grant and agreement governing the RSUs granted to Ms. Roberts in January 2017, immediately prior to, but contingent upon, the consummation of the proposed merger with Savara, all outstanding and unexercised stock options held by Ms. Roberts will be cancelled and cease to be exercisable as of such time without any accelerated vesting.
- (10) Consists of 1,273,371 shares of common stock subject to options currently exercisable or exercisable within 60 days of the Evaluation Date. In accordance with the notice of grant and agreement governing the RSUs granted to Dr. Parsley in January 2017, immediately prior to, but contingent upon, the consummation of the proposed merger with Savara, all outstanding and unexercised stock options held by Dr. Parsley will be cancelled and cease to be exercisable as of such time without any accelerated vesting.
- (11) Consists of 602,824 shares of common stock subject to options currently exercisable or exercisable within 60 days of the Evaluation Date. In accordance with the notice of grant and agreement governing the RSUs granted to Ms. Hood in January 2017, immediately prior to, but contingent upon, the consummation of the proposed merger with Savara, all outstanding and unexercised stock options held by Ms. Hood will be cancelled and cease to be exercisable as of such time without any accelerated vesting.

(12) Consists of (a) 1,000,649 shares of common stock subject to options currently exercisable and (b) 294,598 shares of common stock held directly by Dr. Emanuele. The shares of common stock owned by Dr. Emanuele were issued to him in his capacity as a former stockholder of SynthRx, Inc. pursuant to our Agreement and Plan of Merger with SynthRx, Inc., dated February 12, 2011, which we acquired in April 2011. These shares are subject to the Stockholders' Voting and Transfer Restriction Agreement, dated February 12, 2011, pursuant to which Dr. Emanuele agreed, with respect to every action or approval by written consent of our stockholders (subject to limited exceptions), to vote all shares of our common stock beneficially owned by him that were issued pursuant to the terms of the merger agreement in such manner as we direct and granted an irrevocable proxy to us for the duration of such voting agreement. Dr. Emanuele's employment was terminated in October 2016.

(13) Consists of 1,783,775 shares of common stock subject to options currently exercisable. Mr. Gorgas' employment was terminated in December 2016.

(14) Consists of (a) 9,606,355 shares of common stock subject to options currently exercisable or exercisable within 60 days of the Evaluation Date and (b) 172,500 shares of common stock. In accordance with the notices of grant and agreements governing the RSUs granted to our directors and executive officers in January 2017, immediately prior to, but contingent upon, the consummation of the proposed merger with Savara, all outstanding and unexercised stock options held by such individuals will be cancelled and cease to be exercisable as of such time without any accelerated vesting.

Equity Compensation Plan Information

The following table provides information as of December 31, 2016 regarding equity compensation plans previously approved by our stockholders. We do not have any equity compensation plans that have not been approved by our stockholders. All share and per share information included in this table reflects retrospective application of the 1-for-25 reverse split of our outstanding common stock effected on April 23, 2010.

Plan Category	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights	Weighted-Average Exercise Price of Outstanding Warrants and Rights	Number of Securities Remaining Available For Future Issuance Under Equity Compensation Plans (excluding securities reflected in

	(a)	(b)	column (a) (c)
Equity Compensation Plans Approved by Security Holders (1):			
2015 Omnibus Incentive Plan	8,254,927	\$ 0.45	22,401,967
2014 Omnibus Incentive Plan	8,531,219	\$ 0.60	—
2013 Omnibus Incentive Plan	3,171,163	\$ 0.49	—
Amended and Restated 2008 Omnibus Incentive Plan	1,806,877	\$ 1.29	—
2008 Omnibus Incentive Plan	284,317	\$ 4.15	—
2005 Equity Incentive Plan	16,599	\$ 41.58	—
Equity Compensation Plans Not Approved by Security Holders:	—	—	—
Total	22,065,102	\$ 0.66	22,401,967

(1) On June 11, 2015, the 2015 Omnibus Incentive Plan (the “2015 Plan”) was approved by our stockholders and became effective. Upon effectiveness, the 2015 Plan amended, renamed and restated in its entirety the 2014 Omnibus Incentive Plan (the “2014 Plan”), and no awards have been or will be granted under the 2014 Plan after the 2015 Plan became effective. Similarly, when each of the 2014 Plan, the 2013 Omnibus Incentive Plan, the Amended and Restated 2008 Omnibus Incentive Plan and the 2008 Omnibus Incentive Plan was approved by our stockholders and became effective, upon effectiveness, such plan amended, renamed and restated in its entirety the plan that was then in effect, and no awards have since been or will be granted under any plan that was so amended, renamed and restated. In addition, when our stockholders approved the 2008 Omnibus Incentive Plan, the 2005 Equity Incentive Plan was terminated and no awards have since been or will be granted under that plan. Collectively, these prior stockholder-approved plans are referred to as the “Prior Plans.” If any awards granted under the 2015 Plan or under any of the Prior Plans are forfeited, expire or are settled for cash pursuant to the terms of an award, we may use the shares that were subject to the award for new awards under the 2015 Plan to the extent of the forfeiture, expiration or settlement, other than under specified circumstances. The shares will be added to the 2015 Plan as one share for every share of common stock if the

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shares were subject to a stock option or stock appreciation right, and as 1.34 shares for every share of common stock if the shares were subject to an award other than a stock option or stock appreciation right.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

Certain Related-Person Transactions

Except as set forth below and as described in Part III, Item 11 of this report under “Executive Compensation” and “Director Compensation,” since January 1, 2016, there has not been, nor currently are there proposed, any transactions or series of similar transactions in which we were or are to be a participant and the amount involved exceeded or will exceed \$120,000 and in which any of our directors, executive officers, holders of more than 5% of our common stock or any member of the immediate family of any of the foregoing persons, had or will have a direct or indirect material interest.

Indemnification of Officers and Directors

Our certificate of incorporation and our bylaws, each as amended, provide that we will indemnify each of our directors and officers to the fullest extent permitted by the Delaware General Corporation Law. Further, we have entered into indemnification agreements with each of our directors and officers, and we have purchased directors’ and officers’ liability insurance that insures our directors and officers against the cost of defense, settlement or payment of a judgment under certain circumstances.

Merger Agreement with Savara Inc.

Voting Agreements and Lock-Up Agreements

On January 6, 2017, we entered into an Agreement and Plan of Merger with Savara Inc., pursuant to which Victoria Merger Corp., a wholly-owned subsidiary of our company, will merge with and into Savara, with Savara surviving the merger as a wholly-owned subsidiary of our company and Savara stockholders receiving newly issued shares of our common stock in exchange for their Savara stock. The transactions contemplated by the merger agreement will result in a change in control of our company as further described in Part I, Item 1, “Business,” in this report. The merger is expected to close in the second quarter of 2017, subject to the satisfaction or waiver of certain closing conditions, including approval of the merger by our stockholders and the stockholders of Savara. Our board of directors unanimously approved the merger agreement and the transactions contemplated by the merger agreement.

In order to induce Savara to enter into the merger agreement, on January 6, 2017, Brian Culley, our Chief Executive Officer, Brandi Roberts, our Chief Financial Officer, Shana Hood, our General Counsel, and each of our non-employee directors entered into voting agreements with us, pursuant to which, among other things, each of them agreed (solely in his or her capacity as a stockholder) to vote all of his or her shares of our capital stock in favor of the adoption of the merger agreement with Savara and the approval of the merger and the other transactions contemplated by the merger agreement, and any other matter that is reasonably necessary to facilitate the consummation of the merger and the other transactions contemplated by the merger agreement, and against any matter that would reasonably be expected to impede, interfere with, delay, postpone or adversely affect the merger or any of the transactions contemplated by the merger agreement. As of March 2, 2017, the executive officers and directors who are party to these voting agreements owned less than 1% of the outstanding shares of our common stock.

In addition, on January 6, 2017, these officers and directors entered into lock-up agreements with us pursuant to which they agreed not to, except in limited circumstances, (i) offer, pledge, sell, contract to sell, sell any option or contract purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, make any short sale or otherwise transfer or dispose of or lend any shares of our common stock or securities convertible into, exercisable or exchangeable for or that represent the right to receive our common stock whether then owned or thereafter acquired

(such securities referred to as the “Subject Securities”), (ii) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of those securities, (iii) make any demanded for or exercise any right with respect to the registration of any our common stock or any security convertible into or exercisable or exchangeable for our common stock or (iv) publicly disclose the intention to do any of the foregoing (each such restriction referred to as the “lock-up restrictions”). The lock-up restrictions automatically terminate with respect to one-third of an individual’s Subject Securities on each of (i) the six month anniversary of the date of the closing of the merger, (ii) the eight month anniversary of the date of the closing of the merger and (iii) the ten month anniversary of the date of the closing of the merger. On January 21, 2017, we entered into an amendment to the lock-up agreements with our executive officers and directors, pursuant to which those individuals will be permitted to sell shares of common stock acquired upon settlement of RSUs prior to the expiration of the lock-up restrictions, but solely to the extent necessary to fund the payment of tax withholding obligations due with respect to the settlement of those RSUs.

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Interests of Our Directors and Executive Officers in the Proposed Merger

Two of our independent directors are expected to continue as directors of the combined company upon the closing of the merger with Savara. Which two of our independent directors will continue to serve as directors after the merger has not yet been determined.

All of our directors and executive officers are entitled to certain indemnification and liability insurance coverage pursuant to the terms of the merger agreement and coverage pursuant to insurance policies maintained by us.

As discussed in Part III, Item 11 of this report under “Executive Compensation” and “Director Compensation,” we previously entered into severance agreements with our executive officers that provide them with cash severance payments, cash payments intended to cover certain health insurance coverage costs and the acceleration of their outstanding stock option awards in the event their employment is terminated without cause following a change of control of our company. In addition, and also as described in Part III, Item 11 of this report, on January 17, 2017, our board of directors approved certain RSU awards to our executive officers and directors, which were subsequently granted and will vest in full upon the consummation of the merger with Savara, and a cash bonus award for our executive officers, payable upon the consummation of the merger.

Policies and Procedures for Review and Approval Related Person Transactions

Pursuant to the written charter of the audit committee of our board of directors, the audit committee is responsible for reviewing and approving, any proposed transaction that would require disclosure pursuant to Item 404 of Regulation S-K. If the audit committee approves a related-person transaction, it will regularly review the status of the transaction and any proposed material change to the previously approved terms or conditions.

Director Independence

Our board of directors has determined that each of Dr. Dittrich and Messrs. Greenleaf, Pauls and Ramsay, is an “independent director” as such term is defined in Section 803(A)(2) of the NYSE MKT LLC Company Guide.

Item 14. Principal Accounting Fees and Services.

Fees of Independent Registered Public Accounting Firm for Fiscal Years 2016 and 2015

In March 2016, the audit committee of our board of directors selected Mayer Hoffman McCann P.C. (“MHM”) as our independent registered public accounting firm for the fiscal year ended December 31, 2016. Prior to selecting MHM, PricewaterhouseCoopers LLP (“PwC”) was engaged as our independent registered public accounting firm and PwC audited our consolidated financial statements for the fiscal year ended December 31, 2015.

The following table presents the fees for professional services rendered by MHM for the audit of our consolidated financial statements for the fiscal year ended December 31, 2016 and by PwC for the audit of our consolidated financial statements for the fiscal year ended December 31, 2015. During those periods, no other category of services was provided to us by MHM or PwC.

	2016	2015
Audit Fees (1)	\$220,000	\$484,552
Audit-Related Fees	—	—
Tax Fees	—	—
All Other Fees	—	—
Total	\$220,000	\$484,552

(1) “Audit Fees” were principally for audit work performed on our consolidated financial statements and internal control over financial reporting, but also include fees for professional services provided in connection with the review of financial statements included in our quarterly reports and our registration statements filed with the SEC, and related services normally provided in connection with statutory and regulatory filings and engagements, such as providing comfort and consent letters.

MHM has advised us that MHM leases substantially all of its personnel, who work under the control of MHM’s shareholders, from wholly-owned subsidiaries of CBIZ, Inc., in an alternative practice structure. Accordingly, substantially all of the hours expended on MHM’s engagement to audit our consolidated financial statements and internal control over financial reporting for the year ended December 31, 2016 were attributed to work performed by persons other than MHM’s full-time, permanent employees.

Pre-Approval Policies and Procedures

Pursuant to its written charter, the audit committee must approve, in advance of their performance, all audit, review and attest services and all permissible non-audit services (including any permissible tax or internal control-related services) to be provided by our independent registered public accounting firm. The audit committee may pre-approve services as part of its approval of the scope of the engagement of the independent registered public accounting firm or on an individual case-by-case basis. The audit committee considers whether the provision of any non-audit service is compatible with maintaining the independence of our auditors. The audit committee’s charter provides that it may adopt policies and procedures for the pre-approval of permissible services, which may include delegation of authority to a designated member or members of the audit committee to approve permissible services so long as any such approvals are disclosed to the full audit committee.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) Documents Filed. The following documents are filed as part of this report:

(1) Financial Statements. The following reports of Mayer Hoffman McCann P.C. and PricewaterhouseCoopers LLP and financial statements:

• Reports of Mayer Hoffman McCann P.C., Independent Registered Public Accounting Firm for the year ended December 31, 2016

• Report of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm for the years ended December 31, 2015 and 2014

• Consolidated Balance Sheets as of December 31, 2016 and 2015

• Consolidated Statements of Operations and Comprehensive Loss for the years ended December 31, 2016, 2015 and 2014

• Consolidated Statements of Stockholders' Equity for the years ended December 31, 2016, 2015 and 2014

• Consolidated Statements of Cash Flows for the years ended December 31, 2016, 2015 and 2014

• Notes to Consolidated Financial Statements

(2) Financial Statement Schedules. See subsection (c) below.

(3) Exhibits. See subsection (b) below.

(b) Exhibits. The exhibits filed or furnished with this report are set forth on the Exhibit Index immediately following the signature page of this report, which Exhibit Index is incorporated herein by reference.

(c) Financial Statement Schedules. All schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

Item 16. Form 10-K Summary.

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) 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.

Date: March 6, 2017 Mast Therapeutics, Inc.

By: /s/ Brian M. Culley
 Brian M. Culley
 Chief Executive Officer and Director

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Brian M. Culley and Brandi L. Roberts, and each of them acting individually, as his/her true and lawful attorneys-in-fact and agents, each with full power to act alone, with full powers of substitution and resubstitution, for him/her and in his/her name, place and stead, in any and all capacities, to sign any and all amendments to this annual report on Form 10-K, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully for all intents and purposes as he/she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them or their substitute or resubstitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Brian M. Culley	Chief Executive Officer and Director	March 6, 2017
Brian M. Culley	(Principal Executive Officer)	
/s/ Brandi L. Roberts	Chief Financial Officer and Senior Vice President	March 6, 2017
Brandi L. Roberts	(Principal Financial and Accounting Officer)	
/s/ Matthew Pauls	Chairman of the Board	March 6, 2017
Matthew Pauls		
/s/ Howard C. Dittrich	Director	March 6, 2017
Howard C. Dittrich		
/s/ Peter Greenleaf	Director	March 6, 2017
Peter Greenleaf		

/s/ David A. Ramsay Director

March 6, 2017

David A. Ramsay

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Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders

Mast Therapeutics, Inc. and Subsidiaries

We have audited the accompanying consolidated balance sheet of Mast Therapeutics, Inc. and Subsidiaries (the "Company") as of December 31, 2016, and the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for the year ended December 31, 2016. These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audit provides a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of Mast Therapeutics, Inc. and Subsidiaries as of December 31, 2016, and the results of their operations and their cash flows for the year ended December 31, 2016, in conformity with accounting principles generally accepted in the United States of America.

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has suffered recurring losses and insufficient working capital to fund operations for the next twelve months. These conditions raise substantial doubt about the Company's ability to continue as a going concern. Management's plans in regard to these matters are described in Note 1 to the consolidated financial statements. The consolidated financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from the outcome of this uncertainty.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Mast Therapeutics, Inc. and Subsidiaries' internal control over financial reporting as of December 31, 2016, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO), and our report dated March 6, 2017 expressed an unqualified opinion.

/s/ Mayer Hoffman McCann P.C.

San Diego, CA

March 6, 2017

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Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of

Mast Therapeutics, Inc. and Subsidiaries

We have audited Mast Therapeutics, Inc. and Subsidiaries' (the "Company") internal control over financial reporting as of December 31, 2016, based on criteria established in Internal Control—Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

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In our opinion, Mast Therapeutics, Inc. and Subsidiaries maintained, in all material respects, effective internal control over financial reporting as of December 31, 2016, based on criteria established in Internal Control—Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheet and the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows of Mast Therapeutics, Inc. and Subsidiaries, and our report dated March 6, 2017 expressed an unqualified opinion.

/s/ Mayer Hoffman McCann P.C.

San Diego, California

March 6, 2017

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Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of

Mast Therapeutics, Inc.

In our opinion, the consolidated balance sheet as of December 31, 2015 and the related consolidated statements of operations and comprehensive loss, of stockholders' equity and of cash flows for each of the two years in the period ended December 31, 2015 present fairly, in all material respects, the financial position of Mast Therapeutics, Inc. and its subsidiaries as of December 31, 2015, and the results of their operations and their cash flows for each of the two years in the period ended December 31, 2015, in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these financial statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

As discussed in Note 1 to the consolidated financial statements, the Company has incurred significant operating losses since inception and will require additional financing to fund future operations. Management's plans in regard to these matters are also described in Note 1.

/s/ PricewaterhouseCoopers LLP

San Diego, California

March 14, 2016

Mast Therapeutics, Inc. and Subsidiaries

Consolidated Balance Sheets

(in thousands, except for share and par value data)

	December 31, 2016	December 31, 2015
Assets		
Current assets:		
Cash and cash equivalents	\$8,542	\$23,052
Investment securities	2,740	17,929
Prepaid expenses and other current assets	903	1,271
Total current assets	12,185	42,252
Property and equipment, net	99	226
In-process research and development	2,500	8,549
Goodwill	3,007	3,007
Other assets	131	183
Total assets	\$17,922	\$54,217
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	\$626	\$2,600
Accrued liabilities	1,974	8,152
Accrued compensation and payroll taxes	718	1,430
Debt facility	1,548	10,991
Total current liabilities	4,866	23,173
Long-term lease obligation	17	25
Debt facility, net of current portion	2,285	3,726
Deferred income tax liability	995	3,404
Total liabilities	8,163	30,328
Commitments (Note 12)		
Stockholders' equity:		
Common stock, \$0.001 par value; 500,000,000 shares authorized; 254,746,933 and 163,614,297 shares issued and outstanding at December 31, 2016 and 2015, respectively	255	164
Additional paid-in capital	320,576	298,715
Accumulated other comprehensive income/(loss)	1	(17)
Accumulated deficit	(311,073)	(274,973)
Total stockholders' equity	9,759	23,889
Total liabilities and stockholders' equity	\$17,922	\$54,217

See accompanying notes to consolidated financial statements.

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Mast Therapeutics, Inc. and Subsidiaries

Consolidated Statements of Operations and Comprehensive Loss

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

	Years ended December 31,		
	2016	2015	2014
Revenues	\$128	\$—	\$—
Operating expenses:			
Research and development	20,793	28,264	19,435
Selling, general and administrative	9,342	10,963	9,488
Transaction-related expenses	301	—	271
Impairment of IPR&D	6,049	—	—
Depreciation and amortization	99	146	85
Total operating expenses	36,584	39,373	29,279
Loss from operations	(36,456)	(39,373)	(29,279)
Interest income	122	130	69
Interest expense	(2,132)	(603)	—
Other income/(expense), net	(43)	4	508
Loss before income taxes	(38,509)	(39,842)	(28,702)
Income tax benefit	2,409	—	—
Net loss	\$(36,100)	\$(39,842)	\$(28,702)
Net loss per share - basic and diluted	\$(0.17)	\$(0.25)	\$(0.23)
Weighted average shares outstanding - basic and diluted	208,484,370	162,219,116	122,409,183
Comprehensive Loss:			
Net loss	\$(36,100)	\$(39,842)	\$(28,702)
Other comprehensive income/(loss)	18	8	(4)
Comprehensive loss	\$(36,082)	\$(39,834)	\$(28,706)

See accompanying notes to consolidated financial statements.

Mast Therapeutics, Inc. and Subsidiaries

Consolidated Statements of Stockholders' Equity

(in thousands, except for share data)

	Common stock Shares	Amount	Additional paid-in capital	Accumulated other comprehensive income/(loss)	Accumulated deficit	Total stockholders' equity
Balances at January 1, 2014	102,710,286	\$ 103	\$ 254,155	\$ (21)	\$ (206,429)	\$ 47,808
Net loss	—	—	—	—	(28,702)	(28,702)
Sale of common stock and pre-funded warrants, net of offering costs of \$2,095	51,644,288	51	34,203	—	—	34,254
Issuance of stock in Aires acquisition	5,103,702	5	3,265	—	—	3,270
Share-based compensation expense - employee options	—	—	2,032	—	—	2,032
Warrant exercise	100	0	0	—	—	0
Other comprehensive loss	—	—	—	(4)	—	(4)
Balances at December 31, 2014	159,458,376	159	293,655	(25)	(235,131)	58,658
Net loss	—	—	—	—	(39,842)	(39,842)
Sale of common stock, net of offering costs of \$142	4,155,921	5	1,993	—	—	1,998
Issuance of warrants in connection with debt facility	—	—	392	—	—	392
Share-based compensation expense - employee options	—	—	2,675	—	—	2,675
Other comprehensive income	—	—	—	8	—	8
Balances at December 31, 2015	163,614,297	164	298,715	(17)	(274,973)	23,889
Net loss	—	—	—	—	(36,100)	(36,100)
Sale of common stock, net of offering costs of \$1,148	77,235,208	77	18,733	—	—	18,810
	—	—	26	—	—	26

Adjustment of warrants in
connection

with amendment to debt facility

Warrant exercises	13,897,428	14	459	—	—	473
Share-based compensation			2,643			2,643
expense - employee options	—	—		—	—	
Other comprehensive income/(loss)	—	—	—	18	—	18
Balances at December 31, 2016	254,746,933	\$ 255	\$ 320,576	\$ 1	\$ (311,073)	\$ 9,759

See accompanying notes to consolidated financial statements.

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Mast Therapeutics, Inc. and Subsidiaries

Consolidated Statements of Cash Flows

(in thousands)

	Years ended December 31,		
	2016	2015	2014
Cash flows from operating activities:			
Net loss	\$(36,100)	\$(39,842)	\$(28,702)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	99	146	85
Gain on bargain purchase	—	—	(486)
Impairment of IPR&D	6,049	—	—
Benefit for deferred tax liability	(2,409)	—	—
Share-based compensation expense related to employee stock options	2,643	2,675	2,032
Write-off of property and equipment	36	6	—
Amortization of debt issuance costs and debt discount	1,009	185	—
Changes in assets and liabilities, net of effect of acquisitions:			
Increase/(decrease) in prepaid expenses and other assets	363	13	(58)
(Decrease)/increase in accounts payable	(1,974)	1,230	406
(Decrease)/increase in accrued liabilities	(6,983)	2,638	2,078
Net cash used in operating activities	(37,267)	(32,949)	(24,645)
Cash flows from investing activities:			
Purchases of certificates of deposit	—	(13,713)	(19,435)
Proceeds from maturities of certificates of deposit	15,207	17,024	16,659
Proceeds from sales of certificates of deposit	—	249	—
Purchases of property and equipment	(8)	(165)	(147)
Security deposit for new lease	—	—	(130)
Cash obtained through acquisition	—	—	3,534
Net cash provided by investing activities	15,199	3,395	481
Cash flows from financing activities:			
Proceeds from borrowings under debt facility	—	15,000	—
Payments made on debt facility	(11,653)	—	—
Costs paid in connection with debt facility	(123)	(193)	—
Proceeds from sale of common stock	19,958	2,140	30,201
Proceeds from sale and exercise of warrants	473	—	6,148
Payments for offering costs	(1,089)	(142)	(2,058)
Payments for capital lease	(8)	(7)	—
Net cash provided by financing activities	7,558	16,798	34,291
Net (decrease)/increase in cash and cash equivalents	(14,510)	(12,756)	10,127
Cash and cash equivalents at beginning of period	23,052	35,808	25,681
Cash and cash equivalents at end of period	\$8,542	\$23,052	\$35,808

See accompanying notes to consolidated financial statements.

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Mast Therapeutics, Inc. and Subsidiaries

Notes to Consolidated Financial Statements

1. Description of Business

Mast Therapeutics, Inc., a Delaware corporation (“Mast Therapeutics,” “we” or “our company”), is a biopharmaceutical company focused on developing clinical-stage therapies for serious or life-threatening diseases. We have devoted substantially all of our resources to research and development (“R&D”) and acquisition of our product candidates. We have not yet marketed or sold any products or generated any significant revenue. Through our acquisition of Aires Pharmaceuticals, Inc. (“Aires”) in February 2014, we acquired AIR001, a sodium nitrite solution for intermittent inhalation via nebulization, which we are developing for the treatment of heart failure with preserved ejection fraction (HFpEF). Through our acquisition of SynthRx, Inc. (“SynthRx”) in 2011, we acquired vepoloxamer (also known as MST-188).

On January 6, 2017, we entered into an Agreement and Plan of Merger and Reorganization with Savara Inc., a privately-held, clinical-stage specialty pharmaceutical company focused on the development and commercialization of novel therapies for the treatment of serious or life-threatening rare respiratory diseases. Pursuant to the merger agreement, subject to the satisfaction or waiver of the conditions set forth in the agreement, including the approval of our stockholders and Savara’s stockholders, our wholly-owned subsidiary, Victoria Merger Corp. (formed for the purpose of this transaction), will merge with and into Savara, with Savara surviving the merger as a wholly-owned subsidiary of our company and Savara stockholders receiving newly issued shares of our common stock in exchange for their Savara stock. The transactions contemplated by the merger agreement will result in a change in control of our company, with approximately 76% of the shares of our common stock outstanding after consummation of the merger expected to be held by the former Savara securityholders and approximately 24% of such shares expected to be held by our stockholders, assuming no adjustments are required under the merger agreement as a result of our net cash at closing being less than zero dollars or changes to our company’s or Savara’s capitalization at closing of the transaction relative to when we entered into the merger agreement. The merger agreement contemplates that, immediately following the merger, the combined company’s name will be changed from “Mast Therapeutics, Inc.” to “Savara Inc.,” the board of directors will consist of seven members, five of which will be the current directors of Savara and two of which will be independent directors designated by us, which are expected to be two of our current independent directors, and the executive officers of the combined company will be designated by Savara with Savara’s Chief Executive Officer, Robert Neville, being the combined company’s Chief Executive Officer, and Savara’s Chief Financial Officer, David Lowrance, being the combined company’s Chief Financial Officer. The transaction is expected to close in the second quarter of 2017. The combined company’s pipeline would include:

- AeroVanc, an inhaled dry-powder vancomycin to treat chronic methicillin-resistant *Staphylococcus aureus* (MRSA) pulmonary infection in cystic fibrosis (CF), which is in preparation for a pivotal Phase 3 clinical study;
- Molgradex, an inhaled nebulized GM-CSF to treat pulmonary alveolar proteinosis (PAP), which is currently in Phase 2/3 development; and
- AIR001, our lead product candidate.

Liquidity as of December 31, 2016

The accompanying consolidated financial statements have been prepared assuming we will continue to operate as a going concern, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. However, our working capital, anticipated operating expenses and net losses and the uncertainties surrounding our ability to raise additional capital as needed, as discussed below, raise substantial doubt about our ability to continue as a going concern. The consolidated financial statements do not include any adjustments to reflect

the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from the outcome of this uncertainty.

We have incurred significant operating losses since inception and have relied on our ability to fund our operations primarily through equity financings and a debt financing. For the years ended December 31, 2016, 2015 and 2014, we incurred losses from operations of \$36.5 million, \$39.4 million and \$29.3 million, respectively, and our net cash used in operating activities was \$37.3 million, \$32.9 million and \$24.6 million, respectively. At December 31, 2016, we had an accumulated deficit of \$311.1 million, our cash, cash equivalents and investment securities totaled \$11.3 million, and our working capital was \$7.3 million. Our planned operating activities call for expenditures over the next 12 months to exceed our working capital as of December 31, 2016 and our ability to raise additional capital as needed is uncertain. We are focused on managing our operating expenses and maintaining adequate capital to run our business through consummation of the proposed merger with Savara. In addition to managing our operating expenses, we are exploring opportunities to monetize our vepoloxamer-related assets prior to consummation of the merger. There can be no assurance that we will be successful in completing the merger with Savara,

monetizing our vepoloxamer-related assets, or maintaining or raising sufficient additional capital to fund continued operations. We expect that our cash, cash equivalents and investment securities as of December 31, 2016, would be sufficient to fund our operations into the second quarter of 2017.

In addition to the uncertainties surrounding our ability to consummate the proposed merger with Savara or to raise additional capital as needed, which raise substantial doubt about our ability to continue as a going concern, our business, operating results, financial condition, and prospects are subject to significant other risks and uncertainties, including, regarding our ability to successfully develop, obtain regulatory approval for, and license or commercialize our product candidates.

Liquidity as of December 31, 2015

The consolidated financial statements as of and for the year ended December 31, 2015 have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. We have incurred significant operating losses since inception and have relied on our ability to fund our operations primarily through equity financings and a debt financing. For the years ended December 31, 2015 and 2014, we incurred losses from operations of \$39.4 million and \$29.3 million, respectively, and our net cash used in operating activities was \$32.9 million and \$24.6 million, respectively. At December 31, 2015, we had an accumulated deficit of \$275.0 million, our cash, cash equivalents and investment securities totaled \$41.0 million, and our working capital was \$19.1 million. As of December 31, 2015, based upon planned operating activities that assumed positive results in the Phase 3 (EPIC) clinical study of vepoloxamer in sickle cell disease and our cash, cash equivalents and investment securities balances and working capital as of December 31, 2015, we intended to raise additional capital before the fourth quarter of 2016 through equity or debt financings and/or through collaborations, including licensing agreements, to fund our operations. Subject to limited exceptions, our loan and security agreement with Hercules prohibited us from incurring indebtedness without Hercules' prior written consent. If we were unable to raise sufficient additional capital before the fourth quarter of 2016, or in the case of negative results from the EPIC study and prepayment to Hercules on July 31, 2016 of \$10 million of the principal balance under our debt facility, we planned to immediately reduce the scope of our operations, including by delaying or discontinuing investment in development and commercialization efforts for vepoloxamer in sickle cell disease and heart failure. In that case, we expected that our cash, cash equivalents and investment securities as of December 31, 2015, together with the net proceeds from the underwritten public offering we completed in February 2016, would be sufficient to fund our operations, as reduced in scope, into the first quarter of 2017.

2. Summary of Significant Accounting Policies

Basis of Presentation

The consolidated financial statements include the accounts of Mast Therapeutics and its wholly-owned subsidiaries, Aires and SD Pharmaceuticals, Inc. ("SD Pharmaceuticals"). All intercompany accounts and transactions have been eliminated in consolidation.

We account for business combinations, such as our acquisitions of SynthRx in April 2011 and Aires in February 2014, in accordance with Accounting Standards Codification ("ASC") Topic 805, Business Combinations ("ASC Topic 805"). ASC Topic 805 establishes principles and requirements for recognizing and measuring the total consideration transferred to and the assets acquired, liabilities assumed and any non-controlling interests in the acquired target in a business combination. ASC Topic 805 also provides guidance for recognizing and measuring goodwill acquired in a business combination; requires purchased in-process research and development ("IPR&D") to be capitalized at fair value as an intangible asset at the time of acquisition; requires acquisition-related expenses and restructuring costs to be recognized separately from the business combination; expands the definition of what constitutes a business; and requires the acquirer to disclose information that users may need to evaluate and understand the financial effect of the

business combination.

Use of Estimates

The preparation of financial statements in conformity with United States generally accepted accounting principles (“U.S. GAAP”) requires management to make estimates and assumptions that affect the amounts reported in our consolidated financial statements and accompanying notes. On an ongoing basis, we evaluate our estimates, including estimates related to R&D expenses, IPR&D, goodwill, and share-based compensation expenses. We base our estimates on historical experience and various other relevant assumptions we believe to be reasonable under the circumstances. Actual results may differ from these estimates.

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Fair Value of Financial Instruments

Our investment securities are carried at fair value and the carrying value of our debt facility approximates fair value (see Note 6). Cash equivalents, prepaid expenses and other current assets, accounts payable and accrued liabilities, are carried at cost, which we believe approximates fair value due to the short-term maturities of these instruments.

Cash Equivalents

We consider all highly liquid investments with original maturities of three months or less at the date of purchase to be cash equivalents. Cash equivalents are carried at cost, which we believe approximates fair value due to the short-term maturities of these instruments. At December 31, 2016 and 2015, we had \$3.5 million and \$15.8 million of cash equivalents, respectively.

Investment Securities

Investment securities are marketable equity or debt securities. All of our investment securities are “available-for-sale” securities and carried at fair value (see Note 6). Fair value for securities with short maturities and infrequent secondary market trades typically is determined by using a curve-based evaluation model that utilizes quoted prices for similar securities. The evaluation model takes into consideration the days to maturity, coupon rate and settlement date convention. Net unrealized gains or losses on these securities are included in accumulated other comprehensive income/(loss), which is a separate component of stockholders’ equity. Realized gains and realized losses are included in other (expense)/income, net while amortization of premiums and accretion of discounts are included in interest income. Interest and dividends on available-for-sale securities are included in interest income. We periodically evaluate our investment securities for impairment. If we determine that a decline in fair value of any investment security is other than temporary, then the cost basis would be written down to fair value and the decline in value would be charged to earnings.

Our investment securities are under the custodianship of a major financial institution and consist of FDIC-insured certificates of deposit. We have classified all of our investment securities as available-for-sale investment securities because we consider them to be highly liquid and available for use, if needed, in current operations. As of December 31, 2016, none of our investment securities had contractual maturity dates of more than one year. As of December 31, 2015, \$2.7 million, or approximately 15%, of our investment securities had contractual maturity dates of more than one year and less than or equal to 18 months, and none were greater than 18 months.

Property and Equipment

Property and equipment are stated at cost, less accumulated depreciation. Property and equipment are depreciated using the straight-line method over the estimated useful lives of the assets, which generally is three to five years. Leasehold improvements are amortized over the economic life of the asset or the lease term, whichever is shorter. Repairs and maintenance are expensed as incurred.

In accordance with ASC Topic 360-10, Property, Plant and Equipment – Overall, we test for recoverability of long-lived assets, including property and equipment, if events or changes in circumstances indicate that the carrying amount for the assets may not be recoverable. If our assessment indicates impairment, we measure the impairment loss as the amount by which the carrying amount exceeds fair value of the assets. Fair value determinations are based on an undiscounted cash flow model or independent appraisals, as appropriate.

Intangible Assets – Goodwill and Acquired In-Process Research & Development

In accordance with ASC Topic 350, Intangibles – Goodwill and Other (“ASC Topic 350”), our goodwill and acquired IPR&D are determined to have indefinite lives and, therefore, are not amortized. Instead, they are tested for impairment annually and between annual tests if we become aware of an event or a change in circumstances that would indicate the carrying value may be impaired. Pursuant to Accounting Standards Update, or ASU, No. 2011-08, Intangibles – Goodwill and Other (Topic 350): Testing Goodwill for Impairment, and No. 2012-02, Intangibles – Goodwill and Other (Topic 350): Testing Indefinite-Lived Intangible Assets for Impairment, we have the option to first assess qualitative factors to determine whether the existence of events or circumstances leads us to determine that it is more likely than not (that is, a likelihood of more than 50%) that our goodwill or our acquired IPR&D is impaired. If we choose to first assess qualitative factors and we determine that it is not more likely than not goodwill or acquired IPR&D is impaired, we are not required to take further action to test for impairment. We also have the option to bypass the qualitative assessment and perform only the quantitative impairment test, which we may choose to do in some periods but not in others.

If we perform a quantitative assessment of goodwill, we utilize the two-step approach prescribed under ASC Topic 350. Step 1 requires a comparison of the carrying value of a reporting unit, including goodwill, to its estimated fair value. We test for impairment at the entity level because we operate on the basis of a single reporting unit. If our carrying value exceeds our fair value, we then perform Step 2 to measure the amount of impairment loss, if any. In Step 2, we estimate the fair value of our individual assets, including identifiable intangible assets, and liabilities to determine the implied fair value of goodwill. We then compare the carrying value of our goodwill to its implied fair value. The excess of the carrying value of goodwill over its implied fair value, if any, is recorded as an impairment charge.

Similarly, if we perform a quantitative assessment of acquired IPR&D, we compare its carrying value to its estimated fair value to determine whether an impairment exists. In previous years, due to a lack of Level 1 or Level 2 inputs (see Note 6, "Fair Value of Financial Instruments"), the Multi-Period Excess Earnings Method, or MPEEM, which is a form of the income approach, was used to estimate the fair value of acquired IPR&D when performing a quantitative assessment. Under the MPEEM, the fair value of an intangible asset is equal to the present value of the asset's projected incremental after-tax cash flows (excess earnings) remaining after deducting the market rates of return on the estimated value of contributory assets (contributory charge) over its remaining useful life. The MPEEM uses primarily Level 3 inputs (see Note 6, "Fair Value of Financial Instruments") and requires us to make long-term projections of revenues and expenses related to development and commercialization of the acquired assets and assumptions regarding the rate of return on contributory assets, the weighted average cost of capital and the probability adjustment factor for estimated future after-tax cash flows. In evaluating potential impairment of our vepoloxamer-related acquired IPR&D as of December 31, 2016, we utilized Level 2 inputs in the form of expressions of interest in the vepoloxamer-related assets received recent to the valuation date to estimate fair value. The excess of the carrying value over its estimated fair value is recorded as an impairment charge.

Any impairment charges are recorded to our consolidated statements of operations and comprehensive loss. Our determinations as to whether, and, if so, the extent to which, goodwill and acquired IPR&D become impaired are highly judgmental and, in the case of applying the MPEEM approach to estimate fair value, are based on significant assumptions regarding our projected future financial condition and operating results, changes in the manner of our use or development of the acquired assets, our overall business strategy, and regulatory, market and economic environment and trends.

We perform our annual impairment testing as of September 30 each year, or, in the case of initially acquired IPR&D, on the first anniversary of the date we acquired it and subsequently on September 30. As of September 30, 2016, no impairment of goodwill or acquired IPR&D was identified. Events and changes in circumstances since September 30, 2016 indicated that the carrying value of the vepoloxamer-related acquired IPR&D may be impaired. Accordingly, we performed a quantitative assessment of vepoloxamer-related acquired IPR&D as of December 31, 2016. We determined there was an impairment and recognized an impairment charge of \$6.0 million in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2016 and reduced the carrying value of the vepoloxamer-related acquired IPR&D from \$6.5 million to \$0.5 million on our consolidated balance sheet as of December 31, 2016. See Note 4, "Goodwill and IPR&D."

Concentration of Credit Risk and Significant Sources of Supply

Financial instruments that potentially subject us to concentrations of credit risk are primarily cash, cash equivalents and investment securities. We have a board-approved investment policy that sets our investment parameters and limitations with objectives of preserving principal and liquidity. Our cash and cash equivalent balances consist primarily of money market accounts under the custodianship of major financial institutions. Investment securities are invested in accordance with our investment policy. We do not have any financial instruments with off-balance-sheet risk of accounting loss.

We rely on single-source, third-party manufacturers and suppliers for production and supply of key components of our product candidates, for production of the final drug products themselves, and, in the case of AIR001, for supply of the drug delivery device. If these single-source, third-party manufacturers and suppliers are unable to continue providing a key component of or the final drug products or the drug delivery device, as applicable, the initiation or progress of any clinical studies of our product candidates may be severely impeded.

Revenue

We recognize revenues from federal government research grants during the period in which we receive the grant funds, or their collection is reasonably assured, and we incur the qualified expenditures. The expenditures are reflected as a component of R&D expense in our consolidated statements of operations and comprehensive loss. In 2016, we received a grant from the National Institute of Neurological Disorders and Stroke of the NIH. We recognized \$128,000 of revenue for the year ended December 31, 2016 related to reimbursement of costs under this grant.

Research and Development Expense

R&D costs are charged to expense as incurred and include, but are not limited to, clinical and nonclinical study costs, research-related manufacturing and related costs, employee salaries and benefits, consulting services fees and share-based compensation cost. Clinical study costs include, but are not limited to, clinical research organization fees, investigator fees, site costs and, as applicable, comparator drug costs. Costs for certain R&D activities, such as research-related manufacturing and clinical studies, are recognized based on an evaluation of the percentage of work completed or the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, duration of the study and/or information provided to us by our vendors on their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the financial statements as prepaid expenses or accrued R&D costs.

Advance payments to third parties, including nonrefundable amounts, for goods and services that will be used or rendered for future R&D activities are deferred and capitalized, then expensed as the services are performed or as the underlying goods are delivered. If we do not expect the services to be rendered or goods to be delivered, any remaining capitalized amounts for nonrefundable advance payments are charged to expense immediately.

Milestone payments that we make in connection with in-licensed technology or product candidates are expensed as incurred when there is uncertainty in receiving future economic benefits from the licensed technology or product candidates. We consider the future economic benefits from the licensed technology or product candidates to be uncertain until such licensed technology is incorporated into products that, or such product candidates, are approved for marketing by the FDA or when other significant risk factors are abated. For accounting purposes, management has viewed future economic benefits for all of our licensed technology or product candidates to be uncertain.

Share-Based Compensation

Share-based compensation cost is measured at the grant date, based on the estimated fair value of the award using the Black-Scholes valuation model, and is recognized as expense over the vesting period on a straight-line basis. Share-based compensation expense recognized in the consolidated statements of operations for the years ended December 31, 2016, 2015 and 2014 is based on awards ultimately expected to vest and has been reduced for estimated forfeitures. This estimate will be revised in subsequent periods if actual forfeitures differ from those estimates. None of our outstanding share-based awards have market or performance conditions.

Patent Costs

Legal costs and other fees incurred in connection with patent prosecution and maintenance are expensed as incurred, as recoverability of such expenditures is uncertain. These costs are recorded as selling, general and administrative expenses in our consolidated statement of operations and comprehensive loss.

Income Taxes

We account for income taxes and the related accounts under the liability method. Deferred tax assets and liabilities are determined based on the differences between the financial statement carrying amounts and the income tax basis of assets and liabilities. A valuation allowance is applied against any net deferred tax asset if, based on available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The tax effects from an uncertain tax position can be recognized in our consolidated financial statements only if the position is more likely than not of being sustained upon an examination by tax authorities. An uncertain income tax position will not be recognized if it has less than a 50% likelihood of being sustained.

We account for interest and penalties related to income tax matters, if any, in income tax expense.

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Comprehensive Income/(Loss)

Comprehensive income or loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources, including unrealized gains and losses on marketable securities and foreign currency translation adjustments. We present comprehensive income/(loss) in our consolidated statement of operations and comprehensive loss.

Net Loss per Common Share

Basic and diluted net loss per common share is calculated by dividing the net loss applicable to common stock for the periods presented by the weighted-average number of common shares outstanding during those periods, respectively, without consideration for outstanding common stock equivalents because their effect would have been anti-dilutive. Common stock equivalents are included in the calculation of diluted earnings per common share only if their effect is dilutive. For the years ended December 31, 2016, 2015 and 2014, our outstanding common stock equivalents consisted of options and warrants to purchase shares of our common stock. The weighted-average number of those common stock equivalents outstanding for each of the periods presented is set forth in the table below:

	Years ended December 31,		
	2016	2015	2014
Warrants	96,432,619	77,355,271	49,217,355
Options	28,953,269	21,514,699	11,760,113

Supplemental Cash Flow Information

	Years ended December 31,		
	2016	2015	2014
	(in thousands)		
Cash paid for interest on debt facility	\$1,210	\$298	\$—
Supplemental disclosures of non-cash investing and financing activities:			
Issuance of common stock for acquisitions	—	—	3,270
Assumptions of liabilities in acquisitions	—	—	1,069
Unrealized loss on investment securities	(18)	(8)	(4)
Warrants issued in connection with debt			
facility	26	392	—
Purchase of equipment under capital lease	—	40	—
Purchases of property and equipment in			
accounts payable	—	2	17
Offering costs included in accounts payable	—	—	36

Recent Accounting Pronouncements

In January 2017, the Financial Accounting Standards Board (“FASB”) issued Accounting Standards Update (“ASU”) No. 2017-01, Business Combinations (Topic 805): Clarifying the Definition of a Business (“ASU 2017-01”), in an effort to clarify the definition of a business with the objective of adding guidance to assist entities with evaluating whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. The amendments of this ASU are effective for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. The adoption of this guidance is not expected to have a material impact on our financial statements.

In March 2016, the FASB issued ASU No. 2016-09, Compensation – Stock Compensation (“ASU 2016-09”), which involves multiple aspects of the accounting for share-based transactions, including income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. For public companies, ASU 2016-09 is effective for fiscal years beginning after December 15, 2016, including interim periods within those fiscal years. We plan to adopt ASU 2016-09 in the first quarter of 2017 for the quarterly period ending March 31, 2017. The adoption of this guidance is not expected to have a material impact on our financial statements.

In February 2016, the FASB issued ASU No. 2016-02, Leases (ASC 842) (“ASU 2016-02”), ASU 2016-02 sets out the principles for the recognition, measurement, presentation and disclosure of leases for both parties to a contract (i.e., lessees and lessors). The new standard requires lessees to classify leases as either finance or operating leases based on the principle of

whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight line basis over the term of the lease, respectively. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less will be accounted for similar to existing guidance for operating leases. ASC 842 supersedes the previous leases standard, ASC 840 Leases. The standard is effective on January 1, 2019, with early adoption permitted. As of December 31, 2016, we have three operating leases, including the lease of our office facility (see Note 12, “Commitments – Operating Leases”). While we are still evaluating this guidance, we anticipate that we would record our operating leases on the balance sheet as right-of-use assets and lease liabilities at the present value of the lease payments to be made over the lease term. We do not expect this guidance to have a material impact on our consolidated statement of operations and comprehensive loss.

In August 2014, the FASB issued ASU No. 2014-15, Presentation of Financial Statements - Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity’s Ability to Continue as a Going Concern (“ASU 2014-15”). The amendments in ASU 2014-15 will require management to assess, at each annual and interim reporting period, the entity’s ability to continue as a going concern and, if management identifies conditions or events that raise substantial doubt about the entity’s ability to continue as a going concern within one year after the date that the financial statements are issued, to disclose in the notes to the entity’s financial statements the principal conditions or events that raised substantial doubt about the entity’s ability to continue as a going concern, management’s evaluation of their significance, and management’s plans that alleviated or are intended to alleviate substantial doubt about the entity’s ability to continue as a going concern. ASU 2014-15 is effective for annual periods ending after December 15, 2016 and early application is permitted. The amendments in ASU 2014-15 do not have any application to an entity’s financial statements, but only to the related notes. We adopted ASU 2014-15 for the annual period ending December 31, 2016.

3. Acquisition of Aires

On February 27, 2014, we completed the acquisition of Aires in an all-stock transaction pursuant to the terms of an agreement and plan of merger, dated February 7, 2014, by and among us, AP Acquisition Sub, Inc., a wholly-owned subsidiary of ours, Aires, and a stockholders’ representative (the “Merger Agreement”). Aires was a clinical-stage company with its lead product candidate, AIR001 (sodium nitrite) inhalation solution, in Phase 2 studies in pulmonary hypertension. Aires survived the merger transaction as a wholly-owned subsidiary of ours.

Upon completion of the merger, we issued an aggregate of 1,049,706 unregistered shares of our common stock to former Aires stockholders and, in September 2014 after the six-month “holdback” period, we issued an aggregate of 4,053,996 additional unregistered shares of our common stock to former Aires stockholders, all in accordance with the merger agreement. There are no milestone or earn-out payments under the merger agreement; therefore, the total merger consideration was 5,103,702 shares.

We accounted for the acquisition of Aires in accordance with ASC Topic 805. The total purchase price of the acquisition is approximately \$3.3 million. We calculated the purchase price by first multiplying the total number of shares of our common stock issued by \$0.80, which was the closing price per share of our common stock on February 27, 2014, the acquisition date. Then, we applied a discount factor to account for lack of market liquidity due to the restrictions on transfer of the securities for a period of six months following the acquisition in accordance with stockholder agreements we entered into with the former Aires stockholders and the fact that the shares are unregistered and we have no obligation to register them for resale.

Under the acquisition method of accounting, the total purchase price is allocated to Aires’ net tangible and intangible assets and liabilities based on their estimated fair values as of the acquisition date. The table below summarizes the estimated fair values of Aires’ net tangible and intangible assets and liabilities on the acquisition date (in thousands).

Cash and cash equivalents	\$3,534
Prepaid expenses and other assets	86
In-process research and development	2,000
Total assets:	5,620
Accounts payable and accrued liabilities	1,069
Deferred tax liability	795
Total liabilities:	1,864
Net assets acquired	\$3,756

The estimated fair value of the net assets acquired exceeds the purchase price by approximately \$0.5 million. Accordingly, we recognized the \$0.5 million excess as a bargain purchase gain in other income/(expense), net in our condensed consolidated

statements of operations and comprehensive loss. We were able to realize a gain because Aires was in a distressed sale situation. Aires lacked sufficient capital to continue operations and was unable to secure additional capital in the timeframe it required.

Acquired In-Process Research and Development

Acquired IPR&D is the estimated fair value of the AIR001 program as of the acquisition date. We determined that the estimated fair value of the AIR001 program was \$2.0 million as of the acquisition date using the Multi-Period Excess Earnings Method, or MPEEM, which is a form of the income approach. Under the MPEEM, the fair value of an intangible asset is equal to the present value of the asset's projected incremental after-tax cash flows (excess earnings) remaining after deducting the market rates of return on the estimated value of contributory assets (contributory charge) over its remaining useful life.

To calculate fair value of the AIR001 program under the MPEEM, we used probability-weighted, projected cash flows discounted at a rate considered appropriate given the significant inherent risks associated with drug development by clinical-stage companies. Cash flows were calculated based on estimated projections of revenues and expenses related to AIR001 and then reduced by a contributory charge on requisite assets employed. Contributory assets included debt-free working capital, net property and equipment and assembled workforce. Rates of return on the contributory assets were based on rates used for comparable market participants. Cash flows were assumed to extend through a seven-year market exclusivity period. The resultant cash flows were then discounted to present value using a weighted-average cost of capital for companies with profiles substantially similar to that of Aires, which we believe represents the rate that market participants would use to value the assets. We compensated for the phase of development of the program by applying a probability factor to our estimation of the expected future cash flows. The projected cash flows were based on significant assumptions, including the indication in which we will pursue development of AIR001, the time and resources needed to complete the development and regulatory approval of AIR001, estimates of revenue and operating profit related to the program considering its stage of development, the life of the potential commercialized product, market penetration and competition, and risks associated with achieving commercialization, including delay or failure to obtain regulatory approvals to conduct clinical studies, failure of clinical studies, delay or failure to obtain required market clearances, and intellectual property litigation.

Deferred Income Tax Liability

The \$0.8 million recorded as deferred income tax liability resulting from the acquisition reflects the tax impact of the difference between the book basis and tax basis of acquired IPR&D. Such deferred income tax liability cannot be used to offset deferred tax assets when analyzing our valuation allowance as the acquired IPR&D is considered to have an indefinite life until we complete or abandon development of AIR001.

4. Goodwill and IPR&D

At December 31, 2016 and 2015, our goodwill and IPR&D consisted of the following (in thousands):

	December 31,	
	2016	2015
Goodwill	\$3,007	\$3,007

IPR&D

Acquired IPR&D related to SynthRx acquisition (vepoloxamer)	500	6,549
Acquired IPR&D related to Aires acquisition (AIR001)	2,000	2,000
Total Goodwill and IPR&D	\$5,507	\$11,556

Our goodwill represents the difference between the total purchase price for SynthRx and the aggregate fair values of tangible and intangible assets acquired, less liabilities assumed.

Our acquired IPR&D related to the Aires acquisition reflects the estimated fair value of the AIR001 program as of the date we acquired Aires. We have not identified any impairment to that carrying value. Our acquired IPR&D related to the SynthRx acquisition as of December 31, 2016 reflects the estimated of the fair value of the vepoloxamer-related assets as of the date we acquired SynthRx. As discussed below, we determined the carrying value of the acquired IPR&D related to the SynthRx acquisition (vepoloxamer) was impaired as of December 31, 2016 and reduced its carrying value from \$6.5 million to \$0.5 million as of December 31, 2016.

We test our goodwill and acquired IPR&D for impairment annually as of September 30, or, in the case of initially acquired IPR&D, on the first anniversary of the date we acquired it and subsequently on September 30, and between annual tests if we become aware of an event or a change in circumstances that would indicate the carrying value may be impaired.

We performed a quantitative assessment of our goodwill as of September 30, 2016. We tested for impairment at the entity level because we operate on the basis of a single reporting unit. A quantitative assessment of goodwill utilizes a two-step approach. We first compared our carrying value, including goodwill, to our estimated fair value. If the carrying value had exceeded the estimated fair value, we would have performed Step 2 to measure the amount of any impairment charge. As the carrying value did not exceed estimated fair value, we did not perform Step 2 and concluded that no impairment charge for goodwill is required. We are not aware of an event or change in circumstances since September 30, 2016 that would indicate that our goodwill may be impaired.

We performed a qualitative assessment of our acquired IPR&D related to the Aires acquisition (AIR001) as of September 30, 2016. We noted no events or circumstances that would lead us to determine that the carrying value of that acquired IPR&D exceeds its fair value. Therefore, we concluded that no impairment charge is required. We are not aware of an event or change in circumstances that would indicate that the acquired IPR&D related to the Aires acquisition may be impaired as of December 31, 2016.

We performed a quantitative assessment of our acquired IPR&D related to the SynthRx acquisition (vepoloxamer) as of September 30, 2016. As of that assessment date, due to a lack of Level 1 or Level 2 inputs (see Note 6, “Fair Value of Financial Instruments”), the Multi-Period Excess Earnings Method, or MPEEM, which is a form of the income approach, was used to estimate the fair value of the vepoloxamer-related acquired IPR&D. Under the MPEEM, the fair value of an intangible asset is equal to the present value of the asset’s projected incremental after-tax cash flows (excess earnings) remaining after deducting the market rates of return on the estimated value of contributory assets (contributory charge) over its remaining useful life. The MPEEM uses primarily Level 3 inputs (see Note 6, “Fair Value of Financial Instruments”). We used the MPEEM based on assumptions for development of vepoloxamer in ischemic stroke to evaluate potential impairment as of September 30, 2016 and concluded no impairment charge was required.

Events and changes in circumstances since September 30, 2016 indicated that the carrying value of the vepoloxamer-related acquired IPR&D may be impaired. We considered that during our evaluation of strategic opportunities for our company we identified limited opportunities to monetize the vepoloxamer-related assets and our proposed merger partner, Savara, did not ascribe any significant value to those assets in negotiation of the merger agreement and agreed to allow us to continue to seek to monetize those assets during the pre-closing period of the proposed merger, including through a sale or other transfer of all or substantially all of the assets. We also considered the limited time before anticipated closing of the proposed merger and believe it is not appropriate to consider potential long-term cash flows that may only be achieved with significant further clinical development. We performed a quantitative assessment of the vepoloxamer-related acquired IPR&D as of December 31, 2016 utilizing Level 2 inputs in the form of expressions of interest in the vepoloxamer-related assets received recent to the valuation date to estimate fair value. Based on those expressions of interest, we determined that the estimated fair value of our vepoloxamer-related acquired IPR&D was \$0.5 million as of December 31, 2016. Accordingly, the carrying value of that acquired IPR&D was reduced from \$6.5 million to \$0.5 million on our consolidated balance sheet as of December 31, 2016, and an impairment charge of \$6.0 million was recorded in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2016.

5. Investment Securities

At December 31, 2016 and 2015, our investment securities were as follows (in thousands):

	December 31,	
	2016	2015
Fair value of investment securities	\$2,740	\$17,929

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Cost basis of investment securities	2,739	17,946
	Years ended	
	December 31,	
	2016	2015
Net unrealized (gains)/losses on investment securities	\$(1)	\$17

6. Fair Value of Financial Instruments

Our cash equivalents are recorded at cost plus accrued interest, which approximates fair value. Our investment securities are carried at fair value. The fair value of financial assets and liabilities is measured under a framework that establishes “levels” which are defined as follows: (i) Level 1 fair value is determined from observable, quoted prices in active markets for identical assets or liabilities; (ii) Level 2 fair value is determined from inputs, other than Level 1 inputs, that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other

inputs that are observable or can be corroborated by observable market data for substantially the full term of the asset or liability; and (iii) Level 3 fair value is determined using the entity's own assumptions about the inputs that market participants would use in pricing an asset or liability.

The following table presents our cash equivalents and investment securities which are measured at fair value on a recurring basis (in thousands):

	Total Fair Value	Fair Value Determined Under:		
		(Level 1)	(Level 2)	(Level 3)
At December 31, 2016:				
Cash equivalents	\$3,517	\$3,517	\$—	\$—
Investment securities	\$2,740	\$—	\$2,740	\$—
At December 31, 2015:				
Cash equivalents	\$15,799	\$15,799	\$—	\$—
Investment securities	\$17,929	\$—	\$17,929	\$—

We believe that our debt facility bears interest at a rate that approximates prevailing market rates for instruments with similar characteristics and, accordingly, the carrying value of the debt facility approximates fair value. The fair value of our debt facility is determined under Level 2 in the fair value hierarchy.

7. Property and Equipment

Property and equipment at December 31, 2016 and 2015 were as follows (in thousands):

	Useful Lives	December 31,	
		2016	2015
Office furniture, computer and lab equipment	3 - 5 years	\$239	\$493
Computer software	3 years	7	16
Leasehold improvements	1 year	44	44
Equipment in progress	n/a	—	12
		290	565
Less: accumulated depreciation and amortization		(191)	(339)
Property and equipment, net		\$99	\$226

Equipment in progress represents the cost of lab equipment not yet available for service as of December 31, 2015. These items are depreciated over their applicable useful lives once they are available for service.

Depreciation and amortization expense was \$99,000, \$146,000 and \$85,000 for the years ended December 31, 2016, 2015 and 2014, respectively.

Write-offs of property and equipment were \$36,000, \$6,000 and \$0 for the years ended December 31, 2016, 2015 and 2014, respectively. Write-offs primarily represent disposals of laboratory and computer equipment that were no longer being utilized. All write-offs are recorded under other income/(expense), net on our consolidated statements of

operations and comprehensive loss.

We lease certain office equipment under leases classified as capital leases. As of December 31, 2016, the total amount of leased equipment was \$40,000 with accumulated depreciation of \$16,000. Interest rates on the leased equipment range from 8% to 14% per annum. The equipment is being amortized over the life of the leases, which range from three to five years.

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Future commitments under capital leases are as follows (in thousands):

Year Ending December 31,	
2017	\$10
2018	10
2019	9
2020	—
Thereafter	—
Total	\$29

Total imputed interest over the life of the capital leases is \$8,000.

8. Accrued Liabilities

Accrued liabilities at December 31, 2016 and 2015 were as follows (in thousands):

	December 31,	
	2016	2015
Accrued R&D agreements and study expenses	\$1,401	\$7,898
Accrued transaction-related expenses	248	—
Other accrued liabilities	325	254
Total accrued liabilities	\$1,974	\$8,152

9. Debt Facility

Hercules Loan and Security Agreement

In 2015, we borrowed an aggregate of \$15 million pursuant to a Loan and Security Agreement with Hercules Technology III, L.P. and Hercules Capital, Inc. (formerly known as, Hercules Technology Growth Capital, Inc.) (together, “Hercules”), as amended (the “Loan Agreement”). Pursuant to the terms and conditions of the Loan Agreement we received the first advance of \$5 million on August 11, 2015 and the second advance of \$10.0 million (the “Second Advance”) on September 28, 2015.

The Loan Agreement required prepayment of \$10.0 million of the principal balance of the loan and any accrued but unpaid fees and expenses (the “Second Advance Prepayment”) on or before October 14, 2016 unless the Phase 3 clinical study of vepoloxamer in sickle cell disease, known as the EPIC study, demonstrated positive results. Our announcement in September 2016 that EPIC did not achieve its primary or secondary efficacy endpoints triggered the Second Advance Prepayment, which was made in October 2016.

The interest rate for the principal balance under the Loan Agreement is the greater of (i) 8.95% plus the prime rate as reported in The Wall Street Journal minus 3.25%, and (ii) 8.95%, determined on a daily basis. The interest rate as of December 31, 2016 was 9.45%. Monthly payments under the Loan Agreement were interest only until July 1, 2016. On July 1, 2016, we started making monthly payments of principal and interest. Payment will continue through the scheduled maturity date of January 1, 2019. An end of term charge of \$712,500 will be due on the scheduled maturity date and is being accrued through interest expense using the effective interest method.

If we elect to prepay the principal balance under the amended Loan Agreement prior to maturity, a prepayment charge of 1% or 2% of the then outstanding principal balance also will be due, depending upon when the prepayment occurs. No prepayment penalty applied to the Second Advance Prepayment.

Our obligations under the amended Loan Agreement are secured by a first priority security interest in substantially all of our assets, excluding our intellectual property but including the proceeds from the sale, licensing or disposition of our intellectual property. Our intellectual property is subject to customary negative covenants.

In connection with the Loan Agreement, we have paid facility charges of \$225,000, as of December 31, 2016 and a commitment charge of \$25,000. Such charges were accounted for as debt issuance costs and are being amortized to interest expense using the effective interest method through the scheduled maturity date.

In connection with the Loan Agreement, we entered into a Warrant Agreement with Hercules, dated August 11, 2015, as amended by the First Amendment thereto dated September 28, 2015 and the Second Amendment thereto dated February 25, 2016, pursuant to which Hercules has a right to purchase up to 2,272,727 shares of our common stock at an exercise price of

\$0.275 per share. Prior to the Second Amendment to Warrant Agreement, the Warrant Agreement, as amended, provided Hercules a right to purchase up to 1,524,390 shares of our common stock at an exercise price of \$0.41 per share.

The warrants issued to Hercules were valued using the Black-Scholes option pricing model with the following assumptions: volatility of 83%, expected term of five years, risk-free interest rate of 1.2% and a zero dividend yield. The warrant fair value of \$0.4 million has been recorded as a debt discount and is being amortized through interest expense using the effective interest method through the scheduled maturity date. See Note 10 “Capital Stock and Warrants” for further description of the terms of the warrants.

See Note 18, “Subsequent Events,” for additional information on the Loan Agreement and Warrant Agreement with Hercules.

Summary of Carrying Value

The following table summarizes the components of the debt facility carrying value.

	As of December 31, 2016		As of December 31, 2015	
	Short-Term	Long-Term	Short-Term	Long-Term
Potential prepayment to lender	\$—	\$—	\$10,000	\$—
Principal payments to lender and end of term charge	1,521	2,538	874	4,839
Accrued interest	27	—	117	—
Debt issuance costs	—	(180)	—	(776)
Debt discount related to warrants	—	(73)	—	(337)
Carrying value	\$1,548	\$ 2,285	\$10,991	\$ 3,726

Future minimum payments under the debt facility are as follows:

Year Ending December 31,	
2017	\$1,776
2018	1,776
2019	865
Total future minimum payments	4,417
Unamortized interest	(331)
Debt issuance costs and debt discount	(253)
Total minimum payment	3,833
Short-term portion	(1,548)
Long-term debt facility	\$2,285

10. Capital Stock and Warrants

Our certificate of incorporation, as amended, authorizes us to issue 500,000,000 shares of common stock, par value \$0.001 per share, and 1,000,000 shares of preferred stock, par value \$0.001 per share. As of December 31, 2016, 254,746,933 shares of common stock were outstanding and no shares of preferred stock were outstanding.

Underwritten Public Offering of Common Stock and Warrants

In February 2016, we completed an underwritten public offering with gross proceeds of \$8.0 million from the sale and issuance of 29,090,910 units, each consisting of one share of our common stock and one warrant to purchase one share of our common stock. Net proceeds, after deducting underwriting discounts and commissions and other estimated offering expenses, were approximately \$7.3 million. The warrants have an exercise price of \$0.42 per share. We received \$0.4 million in proceeds from the exercise of 816,000 of the warrants in 2016. Subject to certain beneficial ownership limitations, the remaining 28,274,910 warrants are exercisable at any time on or before February 16, 2021.

Underwritten Public Offering of Common Stock, Pre-funded Warrants and Warrants

In November 2014, we completed an underwritten public offering of 30,941,102 shares of our common stock, 13,081,428 “pre-funded” warrants exercisable for up to 13,081,428 shares of our common stock, and 22,011,265 warrants exercisable for up to 22,011,265 shares of our common stock. These securities were offered and sold to the underwriters and the public in units with each Series A unit consisting of one share of our common stock and one-half (0.5) of a warrant and each Series B unit consisting

of one pre-funded warrant and one-half (0.5) of a warrant. Each whole warrant is exercisable for one share of our common stock. We sold an aggregate of 30,941,102 Series A units and 13,081,428 Series B units. The gross proceeds from this financing were \$21.0 million and, after deducting underwriting discounts and commissions and other offering expenses, our net proceeds were \$19.7 million. All of the pre-funded warrants were exercised in 2016 and we received \$0.1 million in proceeds from the exercise of those warrants. Subject to certain beneficial ownership limitations, the warrants with an exercise price of \$0.75 per share are exercisable at any time on or before November 12, 2019.

“At the Market” Equity Offering Program

In February 2014, we entered into a sales agreement with Cowen and Company, LLC (“Cowen”), to sell shares of our common stock, with aggregate gross sales proceeds of up to \$30 million, from time to time, through an “at the market,” or ATM, equity offering program (the “2014 Sales Agreement”), under which Cowen acted as sales agent. In August 2015, we terminated the 2014 Sales Agreement upon entry into a new sales agreement with Cowen to sell shares of our common stock, with aggregate gross sales proceeds of up to \$30 million, from time to time, through an ATM program. As of December 31, 2016, we had sold and issued an aggregate of 73,003,405 shares at a weighted-average sales price of \$0.40 per share under the ATM programs for aggregate gross proceeds of \$29.4 million and \$28.1 million in net proceeds, after deducting sales agent commission and discounts and our other offering costs. As of December 31, 2016, approximately \$18.0 million remains available under the ATM program (on a gross proceeds basis).

Shares Issuable to Former SynthRx Stockholders Upon Achievement of Milestones

In April 2011, we acquired SynthRx as a wholly-owned subsidiary through a merger transaction in exchange for shares of our common stock and rights to additional shares of our common stock upon achievement of specified milestones related to the development of vepoloxamer in sickle cell disease. The merger agreement requires us to issue up to an aggregate of 12,478,050 additional shares of our common stock to the former SynthRx stockholders if and when the development of vepoloxamer achieves the following milestones: (a) 3,839,400 shares upon acceptance for review by the U.S. Food and Drug Administration (“FDA”) of a new drug application (“NDA”) covering the use of purified poloxamer 188 for the treatment of sickle cell crisis in children and (b) 8,638,650 shares upon approval of such NDA by the FDA. Because we have determined not to pursue development of vepoloxamer in sickle cell disease, it is unlikely that these milestones will be achieved and that any of these shares will be issued.

Warrant Exercises

During the year ended December 31, 2016, we issued the following shares of our common stock upon exercise of outstanding warrants and received aggregate net proceeds of \$0.5 million:

- 816,000 shares upon exercise of outstanding warrants with exercise price of \$0.42 per share; and
- 13,081,428 shares upon exercise of outstanding warrants with exercise price of \$0.01 per share.

Warrants

At December 31, 2016, outstanding warrants to purchase shares of common stock are as follows:

Shares Underlying	Expiration Date
-------------------	-----------------

Outstanding Warrants	Exercise Price	
28,097,400	\$ 0.650	June 2018
22,011,265	\$ 0.750	November 2019
2,272,727	\$ 0.275	August 2020
28,274,910	\$ 0.420	February 2021
80,656,302		

Warrants Issued to Hercules

In connection with the Loan Agreement, we entered into a Warrant Agreement with Hercules Technology III, L.P., dated August 11, 2015, as amended by the First Amendment thereto dated September 28, 2015 and the Second Amendment thereto dated February 25, 2016, pursuant to which Hercules has a right to purchase up to 2,272,727 shares of our common stock at an exercise price of \$0.275 per share. Prior to the Second Amendment to Warrant Agreement, the Warrant Agreement, as amended, provided Hercules a right to purchase up to 1,524,390 shares of our common stock at an exercise price of \$0.41 per share. Hercules may exercise its warrants at any time, or from time to time, through August 11, 2020.

The Warrant Agreement, as amended, provides for adjustment to the exercise price and number of shares subject to Hercules' warrants in the event of a merger event, reclassification of our common stock, subdivision or combination of our common stock, or certain dividend payments. Upon exercise, the aggregate exercise price may be paid, at Hercules' election, in cash or on a net issuance basis, based upon the fair market value of our common stock at the time of exercise. If the fair market value of our common stock is greater than the exercise price of the warrants as of immediately before their expiration, to the extent the warrants are not previously exercised in full, the warrants shall be deemed automatically exercised on a net issuance basis as of immediately before their expiration.

See Note 18 "Subsequent Events" for additional information on the warrants issued to Hercules.

11. Equity Incentive Plans

Our equity-based incentive plan, which is stockholder-approved, is intended to encourage ownership of shares of common stock by our directors, officers, employees, consultants and advisors and to provide additional incentive for them to promote the success of our business through the grant of share-based awards. At December 31, 2016, our equity-based incentive plan consisted of the 2005 Equity Incentive Plan (the "2005 Plan") and the 2008 Omnibus Incentive Plan (the "Original 2008 Plan"), which has been amended, restated and renamed four times, first in June 2011 as the Amended and Restated 2008 Omnibus Incentive Plan, then in June 2013 as the 2013 Omnibus Incentive Plan, then in June 2014 as the 2014 Omnibus Incentive Plan and finally in June 2015 as the 2015 Omnibus Incentive Plan (the "2015 Plan"). Following approval by our stockholders of each amendment and restatement of the Original 2008 Plan, no awards have been or will be granted under the terms of the plan in effect immediately prior to such amendment and restatement. In prior years, our stockholder-approved, equity-based incentive plans included the 2005 Employee Stock Purchase Plan. In May 2015, our 2005 Employee Stock Purchase Plan, which had never been implemented, expired.

During the years ended December 31, 2016, 2015 and 2014, all awards granted under our equity-based incentive plans were stock options. The share-based compensation expense from all stock options granted that has been charged to our consolidated statements of operations and comprehensive loss in those periods was as follows (in thousands):

	Years ended December 31,		
	2016	2015	2014
Selling, general and administrative expense	\$1,749	\$2,077	\$1,607
Research and development expense	894	598	425
Share-based compensation expense	\$2,643	\$2,675	\$2,032

For the year ended December 31, 2015, we recognized a \$0.3 million expense in our selling, general and administrative expenses related to share-based compensation expense as a result of the departure of our former president and chief operating officer in February 2015. Termination of the former officer's employment triggered accelerated vesting of a portion of his outstanding, unvested stock options that resulted in \$0.4 million of additional share-based compensation expense, but this additional expense was offset by a \$0.1 million reduction in share-based compensation expense that resulted from cancellation of the remaining, unvested portion of the former officer's outstanding stock options.

2015 Omnibus Incentive Plan

The 2015 Plan provides for the grant of incentive and non-statutory stock options, as well as share appreciation rights, restricted shares, restricted share units, performance units, shares and other share-based awards. Share-based awards are subject to terms and conditions established by our board of directors or the compensation committee of our board

of directors.

As of December 31, 2016, the maximum aggregate number of shares of our common stock available for grant under the 2015 Plan was 22,401,967 shares. Shares of common stock that are subject to awards granted under the 2015 Plan shall be counted against the shares available for issuance under this plan as one share for each share subject to a stock option or stock appreciation right and as 1.34 shares for each share subject to an award other than a stock option or a stock appreciation right. If any shares of common stock subject to an award granted under any of our stockholder-approved, equity-based incentive plans are forfeited, or an award expires or is settled for cash pursuant to the terms of an award, the shares subject to the award may be used again for awards under the 2015 Plan to the extent of the forfeiture, expiration or cash settlement. The shares of common stock will be added back as one share for every share of common stock if the shares were subject to a stock option or stock appreciation right, and as 1.34 shares for every share of common stock if the shares were subject to an award other than a stock option or stock appreciation right. However, the following shares of common stock will not be added to the shares available for issuance under the 2015 Plan: (i) shares tendered or withheld in payment of the purchase price of a stock option, (ii) shares tendered or withheld to satisfy any tax withholding obligation with respect to any award, (iii) shares subject to a stock

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appreciation right that are not issued in connection with the stock settlement of the stock appreciation right on exercise thereof, and (iv) shares reacquired by us on the open market or otherwise using cash proceeds from the exercise of stock options. Shares of common stock under awards made in assumption of or in substitution or exchange for awards previously granted, or the right or obligation to make future awards, in each case by a company acquired by us, or with which we combine, will not reduce the number of shares available for issuance under the 2015 Plan. In addition, if a company acquired by us, or with which we combine, has shares available under a pre-existing plan approved by its stockholders and not adopted in contemplation of such acquisition or combination, the shares available for issuance under such plan (as adjusted, to the extent appropriate, using the exchange or other adjustment or valuation ratio of formula applied to determine the consideration payable to stockholders in the acquisition or combination) may be used for awards under the 2015 Plan and will not reduce the number of shares of common stock available for issuance under the 2015 Plan; provided, however that awards using such available shares shall not be made after the date awards or grants could have been made under the pre-existing plan, absent the acquisition or combination, and shall only be made to individuals who were not our employees or directors prior to the acquisition or combination.

Under the 2015 Plan, the purchase price of shares of common stock covered by a stock option cannot be less than 100% of the fair market value of the common stock on the date the stock option is granted. Fair market value of the common stock is generally equal to the closing price for the common stock on the principal securities exchange on which the common stock is traded on the date the stock option is granted (or if there was no closing price on that date, on the last preceding date on which a closing price was reported). Stock option awards generally have ten-year contractual terms and vest over four years based on continuous service; however, the 2015 Plan allows for other vesting periods.

Summary of 2016 Stock Option Activity

The following table summarizes our stock option activity for the year ended December 31, 2016:

	Shares			
	Underlying Option Awards	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Years	Aggregate Intrinsic Value (in thousands)
Outstanding at January 1, 2016	22,902,727	\$ 0.80		
Granted	8,151,263	\$ 0.42		
Exercised	—	\$ —		
Expired/cancelled/forfeited	(8,988,888)	\$ 0.79		
Outstanding at December 31, 2016	22,065,102	\$ 0.66	6.00	\$ —
Options exercisable at December 31, 2016	13,865,407	\$ 0.75	4.90	\$ —
Vested and expected to vest at				
December 31, 2016	21,334,167	\$ 0.67	5.83	\$ —

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The weighted-average grant-date fair value of options granted during the years ended December 31, 2016, 2015 and 2014 was \$0.29, \$0.42 and \$0.50, respectively. As of December 31, 2016, there was approximately \$2.5 million of unamortized compensation cost related to unvested stock option awards, which is expected to be recognized over a weighted-average period of approximately 2.2 years.

Our determination of fair value is affected by our stock price as well as a number of assumptions that require judgment. The fair value of each option award is estimated on the date of grant using the Black-Scholes option-valuation model. The assumptions used in the Black-Scholes option-valuation model and the calculation of share-based compensation for option grants to employees and non-employee directors during the years ended December 31, 2016, 2015 and 2014 are as follows:

	Years ended December 31,		
	2016	2015	2014
Risk-free interest rate	1.1 - 1.9%	1.6 - 1.9%	1.9 - 2.1%
Dividend yield	0.0%	0.0%	0.0%
Expected volatility	81 - 82%	78 - 99%	104 - 112%
Expected term	5.3 - 6.0 years	5.3 - 6.2 years	5.4 - 6.2 years
Forfeiture rate	11%	7%	9%

The risk-free interest rate assumption is based on the U.S. Treasury yield for a period consistent with the expected term of the option in effect at the time of the grant. We have not paid any dividends on common stock since our inception and do not anticipate paying dividends on our common stock in the foreseeable future. The expected option term is computed using the “simplified” method as permitted under the provisions of Staff Accounting Bulletin (“SAB”) 107. SAB 107’s guidance was extended indefinitely by SAB 110. The expected volatility is based on the historical volatility of our common stock based on the daily closing prices. Forfeiture rates are based on the expected forfeiture rates for our unvested stock options, which are based in large part on our historical forfeiture rates, but also on assumptions believed to be reasonable under the circumstances.

In accordance with ASC 718, Compensation – Stock Compensation, share-based compensation expense associated with the non-employee director options is included with employee share-based compensation expense.

12. Commitments

SynthRx Merger Consideration Milestone Payments

In April 2011, we acquired SynthRx in a merger transaction in exchange of shares of our common stock and rights to additional shares of our common stock. Pursuant to the merger agreement, we could issue up to an aggregate of 12,478,050 shares of our common stock to the former SynthRx stockholders if and when the development of vepoloxamer achieves the following milestones: (a) 3,839,400 shares upon acceptance for review by the U.S. Food and Drug Administration (“FDA”) of a new drug application (“NDA”) covering the use of vepoloxamer for the treatment of sickle cell crisis in children and (b) 8,638,650 shares upon approval of such NDA by the FDA. Because we have determined not to pursue development of vepoloxamer in sickle cell disease, it is unlikely that these milestones will be achieved and that any of these shares will be issued.

Operating Leases

We are obligated under operating leases for office space and equipment. We sublease approximately 13,700 square feet of office space for our corporate headquarters in San Diego, California. Our sublease commenced on January 20, 2015 and expires on May 31, 2020. Our monthly rent of \$41,000 escalates by 3% each year on January 20th. During the first year of the sublease, the monthly base rent for approximately 2 1/3 months, or approximately \$96,000, was abated. In July 2014, we made a payment of \$300,000 to the landlord, up to approximately \$170,000 of which was applied to our monthly base rent for months 13, 16, 19 and 24 of the sublease term, subject to certain conditions. The remaining \$130,000 is held by the landlord as a security deposit. Rent expense for our office space is recognized on a straight-line basis.

We lease office equipment under a lease that expires in 2019.

Rent expense was approximately \$537,000, \$508,000 and \$334,000 during the years ended December 31, 2016, 2015 and 2014, respectively.

Future rental commitments under all operating leases are as follows (in thousands):

Year Ending December 31,	
2017	\$ 489
2018	547
2019	557
2020	237

Thereafter	—
Total	\$ 1,830

13. Income Taxes

Due to our historical net loss position, we have recorded a full valuation allowance against net deferred tax assets, therefore there is typically no provision or benefit for income taxes recorded. For the year ended December 31, 2016, we have an income tax benefit of \$2,409,000 related to the impairment of the indefinite-lived vepoloxamer-related IPR&D. For the years ended December 31, 2015 and 2014, there is no provision or benefit for income taxes recorded.

The income tax benefit is different from that which would be obtained by applying the statutory Federal income tax rate of 34% to income before income tax expense. The items causing this difference for the years ended December 31, 2016, 2015 and 2014 are as follows:

	Years ended December 31,		
	2016	2015	2014
	(in thousands)		
Income tax benefit at federal statutory rate	\$(13,092)	\$(13,546)	\$(9,758)
Orphan drug credit / R&D credit	(4,458)	(7,530)	(4,575)
Stock options	543	594	278
Other	(430)	187	(213)
Change in federal valuation allowance	15,028	20,295	14,268
Total	\$(2,409)	\$—	\$—

Deferred income taxes reflect the net tax effect of temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of deferred tax assets and liabilities at December 31, 2016 and 2015 are as follows:

	Years ended December 31,	
	2016	2015
	(in thousands)	
Deferred tax assets:		
Accrued expenses	\$179	\$619
Stock options under ASC 718	3,029	2,610
Net operating loss carry forwards	42,489	31,649
Income tax credit carry forwards	26,328	19,369
Property and equipment	5	20
Intangibles	778	895
Other	118	69
Total deferred tax assets	72,926	55,231
Less: valuation allowance	(72,926)	(55,231)
Total deferred tax assets, net of valuation allowance	—	—
Deferred tax liabilities:		
Acquired intangibles	(995)	(3,404)
Total deferred tax assets/liabilities, net of valuation allowance	allowance	\$(995) \$(3,404)

We have established a full valuation allowance against our net deferred tax assets due to uncertainty surrounding the realization of such assets. Management has determined it is more likely than not that the deferred tax assets are not realizable due to our historical loss position.

As a result of our acquisitions of SynthRx and Aires during 2011 and 2014, respectively, we recorded deferred tax liabilities. These deferred tax liabilities reflect the tax impact of the differences between the book basis and tax basis of acquired IPR&D that has not yet reached feasibility. Such deferred tax liabilities cannot be used to offset deferred tax assets when analyzing our end of year valuation allowance as the acquired IPR&D is considered to have an indefinite life until we complete or abandon development. The deferred tax liabilities were recorded as an offset to goodwill or gain on bargain purchase, recorded as part of the SynthRx and Aires acquisitions, respectively. As of December 31, 2016, we determined that our vepoloxamer-related IPR&D was impaired and the carrying value of such IPR&D was reduced from \$6.5 million to \$0.5 million (see Note 4, "Goodwill and IPR&D," for additional information). Accordingly, we reduced our related deferred tax liability from \$2.6 million to \$0.2 million. The \$2.4 million reduction was recorded as an income tax benefit on our consolidated statement of operations and comprehensive loss. There was no change to the deferred tax liability of \$0.8 million related to our AIR001-related IPR&D. Our total deferred tax liability as of December 31, 2016 was \$1.0 million.

Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or IRC, limit our ability to use net operating loss carry forwards and R&D tax credit carry forwards ("tax attribute carry forwards") to offset future taxable income or income tax, respectively, if we experience a cumulative change in ownership of more than 50% within a three-year testing period. We

completed a formal study through the year ended December 31, 2011 and determined ownership changes within the meaning of IRC Section 382 had occurred. We adjusted our tax attribute carry forwards and deferred tax assets accordingly. As the deferred tax assets associated with the tax attribute carry forwards were fully offset by a valuation allowance, a corresponding reduction in the Company's valuation allowance was also recorded, resulting in no income tax impact. We completed a formal study to determine whether an ownership change, within the meaning of IRC Section 382, occurred during 2012, 2013 or 2014, and no ownership changes were identified.

As of December 31, 2016, we had federal and California net operating loss carry forwards of \$105.3 million and \$114.9 million, respectively. These tax loss carry forwards begin to expire in 2031 if unused. As of December 31, 2016, we also had federal R&D/orphan drug and California R&D tax credit carry forwards of \$25.6 million and \$1.1 million, respectively. The aforementioned federal tax credits will begin to expire in 2031. The California R&D tax credits do not expire.

In accordance with authoritative guidance, the impact of an uncertain income tax position on the income tax return must be recognized at the largest amount that is more-likely-than-not to be sustained upon audit by the relevant taxing authority. An uncertain income tax position will not be recognized if it has less than a 50% likelihood of being sustained. As of December 31, 2016, we continue to have no unrecognized tax benefits. There are no unrecognized tax benefits included on the balance sheets that would, if recognized, impact the effective tax rate. We do not anticipate there will be a significant change in unrecognized tax benefits within the next 12 months.

Our policy is to recognize interest and/or penalties related to income tax matters in income tax expense. Because we have generated net operating losses since inception, no tax liability, penalties or interest has been recognized for balance sheet or income statement purposes as of and for the years ended December 31, 2016 and 2015.

We are subject to income taxation in the U.S. and the state of California. All of our tax years are subject to examination by the tax authorities due to the carry forward of unutilized net operating losses and R&D tax credits.

14. 401(k) Plan

We have a defined contribution savings plan pursuant to Section 401(k) of the IRC. The plan is for the benefit of all qualifying employees and permits voluntary contributions by employees up to 100% of eligible compensation, subject to the Internal Revenue Service ("IRS") imposed maximum limits. The terms of the plan during 2016, 2015 and 2014 required us to make matching contributions equal to 100% of employee contributions up to 6% of eligible compensation, limited by the IRS-imposed maximum. We incurred total expenses of \$242,000, \$246,000 and \$212,000 in employer matching contributions in 2016, 2015 and 2014, respectively.

15. Restructuring Costs

In the fourth quarter of 2016, as part of restructuring our organization after the Phase 3 clinical study of vepoloxamer in sickle cell disease did not meet its primary efficacy endpoint and we made the decision to discontinue all clinical development of vepoloxamer, we eliminated 18 positions across our company, 16 through involuntary terminations and two due to resignations. As a result, we incurred restructuring costs in the fourth quarter of 2016 of approximately \$0.8 million for one-time employee termination costs, including severance, benefits and related costs. Restructuring costs were recorded as research and development expense (\$0.5 million) and selling, general and administrative expense (\$0.3 million) on the consolidated statements of operations and comprehensive loss for the year ended December 31, 2016. \$0.3 million of the restructuring costs were accrued on our consolidated balance sheet as of December 31, 2016 and paid in January 2017.

16. Segment Information

We operate our business on the basis of a single reportable segment, which is the business of developing therapies for serious or life-threatening diseases. We evaluate our Company as a single operating segment. The majority of our

operating activities and work performed by our employees are currently conducted from a single location in the U.S. We recognized \$128,000 of research grant revenue in 2016. We recognized no revenues in 2015 and 2014.

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17. Summary of Quarterly Financial Data (unaudited)

The following is a summary of the unaudited quarterly results of operations for the years ended December 31, 2016, 2015 and 2014 (in thousands, except per share data):

Quarterly statements of operations data

	Quarters Ended			
	March 31	June 30	September 30	December 31
2016 (unaudited)				
Revenue	\$—	\$—	\$45	\$83
Loss from operations	(10,742)	(10,221)	(7,201)	(8,292)
Net loss	(11,207)	(10,706)	(8,152)	(6,035)
Net loss applicable to common stock	(11,207)	(10,706)	(8,152)	(6,035)
Basic and diluted net loss per share	\$(0.06)	\$(0.05)	\$(0.04)	\$(0.02)
Basic and diluted weighted average number of shares				
of common stock outstanding	178,115	196,554	214,714	244,094
2015 (unaudited)				
Revenue	\$—	\$—	\$—	\$—
Loss from operations	(9,650)	(10,181)	(9,828)	(9,714)
Net loss	(9,616)	(10,151)	(9,912)	(10,162)
Net loss applicable to common stock	(9,616)	(10,151)	(9,912)	(10,162)
Basic and diluted net loss per share	\$(0.06)	\$(0.06)	\$(0.06)	\$(0.06)
Basic and diluted weighted average number of shares				
of common stock outstanding	159,459	162,128	163,614	163,614
2014 (unaudited)				
Revenue	\$—	\$—	\$—	\$—
Loss from operations	(6,839)	(7,202)	(7,884)	(7,354)
Net loss	(6,371)	(7,152)	(7,866)	(7,313)
Net loss applicable to common stock	(6,371)	(7,152)	(7,866)	(7,313)
Basic and diluted net loss per share	\$(0.06)	\$(0.06)	\$(0.06)	\$(0.05)
Basic and diluted weighted average number of shares				
of common stock outstanding	105,054	115,587	123,287	145,257

18. Subsequent Events

Merger Agreement with Savara

As discussed in Note 1, "Description of Business," on January 6, 2017, we entered into an Agreement and Plan of Merger and Reorganization with Savara Inc. and Victoria Merger Corp, a wholly-owned subsidiary we formed for the purpose of this transaction. The completion of the merger and other transactions contemplated by the merger

agreement would constitute a change in control of our company. The material terms of the merger agreement are further described in Part I, Item 1, "Business," in this annual report.

In addition to seeking approval from our stockholders of the merger and our issuance of shares of our common stock to Savara securityholders in consideration for the merger, the merger agreement contemplates that we will seek approval from our stockholders to amend and restate our amended and restated certificate of incorporation to (a) effect a reverse split of our common stock immediately prior to the effective time of the merger and (b) to change our name to "Savara Inc." at the effective time of the merger. The reverse split ratio to be proposed to our stockholders has not been determined.

The transactions contemplated by the merger agreement are expected to close in the second quarter of 2017.

Fifth Amendment to Loan Agreement and Third Amendment to Warrant Agreement with Hercules

Because the proposed merger with Savara would result in a change in control of our company under the Loan Agreement, triggering immediate repayment of the outstanding amount of all principal, accrued interest, accrued, unpaid fees and expenses, together with a prepayment charge of 2% of the principal balance and an end of term charge of \$712,500 (referred to as the

“Change in Control Prepayment Provisions”), on March 3, 2017, we entered into a fifth amendment of the Loan Agreement whereby Hercules agreed that the merger with Savara would not trigger the Change in Control Repayment Provisions and that the loan would remain in place upon its existing terms, including the January 1, 2019 scheduled maturity date, following the consummation of the merger, provided the transaction is completed on or before April 30, 2017. However, beginning on the effective date of the amendment, the combined company will be required to maintain (a) at least \$4 million of cash unless and until our company, Savara or the combined company raise at least \$6 million in net cash proceeds from equity and/or subordinated debt financings on or before April 30, 2017 and (b) at least \$2 million of cash unless and until our company, Savara or the combined company raise at least \$20 million in net cash proceeds from equity and/or subordinated debt financings and/or other financing sources approved by Hercules (including grant amounts) on or before August 31, 2017. This amendment to the Loan Agreement will become effective only upon consummation of the proposed merger. In consideration for the amendment and the consents and waivers provided therein by Hercules, we paid an amendment fee of \$50,000 to Hercules upon execution of the amendment. In addition, concurrently with the amendment to the Loan Agreement, we entered into a third amendment of the Warrant Agreement, pursuant to which, as of the date the amendment to the Loan Agreement becomes effective, the warrant exercise price, which currently is \$0.275 per share, will be reduced to the lesser of (a) \$0.10 per share and (b) if the closing market price of our common stock is lower than \$0.10 per share for three consecutive days between January 6, 2017 and the date of the consummation of the merger with Savara, the lowest three-day volume-weighted average price of our common stock during that period.

See Note 9, “Debt Facility,” and Note 10, “Capital Stock and Warrants,” for additional information about the Loan Agreement and Warrant Agreement.

2017 Compensation and Grants of Restricted Stock Awards

In January 2017, our board of directors, upon the recommendation of its compensation committee, approved a retention/performance bonus for our remaining full-time employees in order to retain, reward and incentivize them to continue their efforts to help our company achieve its goals through the consummation of the proposed merger with Savara. For our executive officers, this bonus is payable 50% in a single-sum cash payment and 50% in a grant of restricted stock units (“RSUs”) under the 2015 Plan. For our other employees, this bonus is payable in a single-sum cash payment. All cash payments and vesting of RSUs are contingent upon consummation of the proposed merger on or before July 6, 2017, continued service with us until that event, and a general release of claims. The RSUs were granted in January 2017. The total amount of cash payable is \$156,000 and the total number of shares of our common stock issuable if the RSUs vest is 980,538.

Additionally, in January 2017, our board of directors, upon the recommendation of its compensation committee, approved the grant of an aggregate of 3,865,964 RSUs to our full-time employees and an aggregate of 234,965 RSUs to our four non-employee directors. All of the RSUs were granted under the 2015 Plan in January 2017. Each RSU represents a right to receive one share of our common stock. Vesting of these RSUs is contingent upon consummation of the proposed merger with Savara on or before July 6, 2017.

In accordance with the notices of grant and agreements governing these RSU awards, all outstanding and unexercised stock options held by the employees and directors will be cancelled immediately prior to, but contingent upon, the consummation of the merger and cease to be exercisable as of such date without any accelerated vesting.

Anticipated Severance Expense

We expect to incur severance expense upon the consummation of the proposed merger with Savara because we anticipate that all of our full-time employees will be involuntarily terminated. In accordance with the Executive Severance Agreements between us and each of our four current executive officers entered into in March 2016 and the

severance arrangements for our non-officer employees approved by our board of directors in January 2017, we expect to make cash severance payments to our existing employees totaling approximately \$1.8 million on or about the date the merger is completed.

Transaction-Related Expenses

We have incurred, and expect to incur additional, significant transaction-related expenses in connection with negotiating and executing the merger agreement with Savara and completing the transactions contemplated by the merger agreement. Transaction-related expenses, which include legal, accounting and financial advisor fees, tail insurance premiums and other service provider costs, are currently estimated to total approximately \$2.6 million. We incurred \$0.3 million of these costs during the fourth quarter of 2016 and recorded that amount as transaction-related expenses on our consolidated statements of operations and comprehensive loss. As of December 31, 2016, \$0.2 million of these costs were accrued on our consolidated balance sheet. We expect to incur the remainder of the anticipated transaction-related expenses in the first half of 2017.

Exhibit Index

Exhibit No.	Description	Incorporated by Reference			Date Filed
		Filed Herewith	Form	File/Film No.	
2.1	Agreement and Plan of Merger and Reorganization, dated January 6, 2017, by and among registrant, Savara Inc. and Victoria Merger Corp.		Form 8-K	001-32157-17515840	01/09/17
2.2	Form of Voting Agreement, by and between the registrant and its directors and officers		Form 8-K	001-32157-17515840	01/09/17
2.3†	Agreement and Plan of Merger, dated February 12, 2011, by and among the registrant, SRX Acquisition Corporation, SynthRx, Inc. and, solely with respect to Sections 2 and 8, the Stockholders' Agent		Form 8-K	001-32157-11752769	04/11/11
2.4†	Agreement and Plan of Merger, dated February 7, 2014, by and among the registrant, AP Acquisition Sub, Inc., Aires Pharmaceuticals, Inc. and, solely with respect to Sections 2.8(b) and 6.3 and Article IX, the Stockholders' Representative, as amended by the Waiver of Closing Conditions, dated February 26, 2014		Form 10-Q	001-32157-14813538	05/05/14
3.1	Composite Amended and Restated Certificate of Incorporation, as amended, of the registrant		Form S-1	333-188870-13873232	05/28/13
3.2	Composite Amended and Restated Bylaws, as amended, of the registrant		Form 10-K	001-32157-14717498	03/26/14
4.1	Form of common stock certificate of the registrant		Form 10-K	001-32157-13702619	03/19/13

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|-----|---|-----------|---------------------|----------|
| 4.2 | Warrant Agent Agreement, dated June 14, 2013, between the registrant and American Stock Transfer & Trust Company, LLC, including the Form of Common Stock Purchase Warrant as Exhibit A | Form 8-K | 001-32157-13917371 | 06/17/13 |
| 4.3 | Form of Warrant Agent Agreement, dated as of November 6, 2014, between the registrant and American Stock Transfer & Trust Company, LLC | Form 8-K | 001-32157-141202528 | 11/07/14 |
| 4.4 | Form of Warrant issued by the registrant on November 12, 2014 | Form 8-K | 001-32157-141202528 | 11/07/14 |
| 4.5 | Warrant Agreement, dated as of August 11, 2015, between the registrant and Hercules Technology III, L.P. | Form 10-Q | 001-32157-151224926 | 11/12/15 |
| 4.6 | First Amendment to Warrant Agreement, dated as of September 28, 2015, between the registrant and Hercules Technology III, L.P. | Form 10-Q | 001-32157-151224926 | 11/12/15 |
| 4.7 | Second Amendment to Warrant Agreement, dated as of February 25, 2016, between the registrant and Hercules Technology III, L.P. | Form 8-K | 001-32157-161468225 | 02/29/16 |
| 4.8 | Third Amendment to Warrant Agreement, dated as of March 3, 2017, between the registrant and Hercules Technology III, L.P. | | | X |
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Exhibit No.	Description	Incorporated by Reference			Date Filed
		Filed Herewith	Form	File/Film No.	
4.9	Form of Warrant Agreement entered into on February 16, 2016 between the registrant and American Stock Transfer & Trust Company, LLC		Form 8-K	001-32157-161407765	02/11/16
4.10	Form of Warrant Certificate for warrants to acquire common stock of the registrant issued by the registrant on February 16, 2016		Form 8-K	001-32157-161407765	02/11/16
10.1	Sales Agreement, dated August 21, 2015, between the registrant and Cowen and Company, LLC		Form 8-K	001-32157-151069175	08/21/15
10.2	Loan and Security Agreement, dated as of August 11, 2015, among the registrant, Hercules Technology III, L.P. and Hercules Technology Growth Capital, Inc.		Form 10-Q	001-32157-151224926	11/12/15
10.3	First Amendment to Loan and Security Agreement, dated as of September 28, 2015, among the registrant, Hercules Technology III, L.P. and Hercules Technology Growth Capital, Inc.		Form 10-Q	001-32157-151224926	11/12/15
10.4	Second Amendment to Loan and Security Agreement, dated as of December 31, 2015, among the registrant, Hercules Technology III, L.P. and Hercules Technology Growth Capital, Inc.		Form 8-K	001-32157-161328864	01/07/16
10.5	Third Amendment to Loan and Security Agreement, dated as of February 25, 2016, among the registrant, Hercules Technology III, L.P. and Hercules Technology Growth Capital, Inc.		Form 8-K	001-32157-161468225	02/29/16

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10.6	Fourth Amendment to Loan and Security Agreement, dated as of July 22, 2016, among the registrant, Hercules Technology III, L.P. and Hercules Technology Growth Capital, Inc.	Form 8-K 001-32157-161782551 07/25/16
10.7	Fifth Amendment to Loan and Security Agreement, dated as of March 3, 2017, among the registrant, Hercules Technology III, L.P. and Hercules Technology Growth Capital, Inc. X	
10.8†	Stockholders' Voting and Transfer Restriction Agreement, dated February 12, 2011, by and among the registrant, each of the principal stockholders of SynthRx, Inc. and, solely with respect to Section 3(c), the Stockholders' Agent	Form 8-K 001-32157-11752769 04/11/11
10.9†	License Agreement, dated June 8, 2004, between SynthRx, Inc. and CytRx Corporation, as amended by that certain Letter Agreement Re: Amendment to License Agreement, dated August 3, 2006, and that certain Agreement and Amendment No. 2 to License Agreement, dated December 1, 2010	Form 8-K 001-32157-11752769 04/11/11
10.10#	2005 Equity Incentive Plan	Form 10-K 001-32157-07697283 03/15/07
10.11#	Form of Stock Option Agreement under the 2005 Equity Incentive Plan	Form S-8 333-126551-05951362 07/13/05
10.12#	Form of Stock Option Agreement under the 2005 Equity Incentive Plan (for director option grants beginning in 2008)	Form 10-K 001-32157-08690952 03/17/08

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Exhibit No.	Description	Incorporated by Reference			Date Filed
		Filed Herewith	Form	File/Film No.	
10.13#	Form of Stock Option Agreement under the 2005 Equity Incentive Plan (for option grants to employees approved in March 2008)		Form 10-Q	001-32157-08820541	05/12/08
10.14#	2008 Omnibus Incentive Plan		Form 8-K	001-32157-08874724	06/02/08
10.15#	Form of Non-Statutory Stock Option Grant Agreement (for directors) under the 2008 Omnibus Incentive Plan		Form 10-Q	001-32157-081005744	08/11/08
10.16#	Form of Non-Statutory/Incentive Stock Option Grant Agreement (for consultants/employees) under the 2008 Omnibus Incentive Plan		Form 10-Q	001-32157-081005744	08/11/08
10.17#	Form of Incentive Stock Option Grant Agreement under the 2008 Omnibus Incentive Plan (for grant to Brian M. Culley in July 2009)		Form 8-K	001-32157-09957353	07/22/09
10.18#	Form of letter, dated January 20, 2010, modifying options granted to Brian M. Culley and Patrick L. Keran in July 2009		Form 8-K	001-32157-10547818	01/26/10
10.19#	Form of Incentive Stock Option Grant Agreement under the 2008 Omnibus Incentive Plan (for grant to Brian M. Culley in January 2010)		Form 8-K	001-32157-10547818	01/26/10
10.20#	Incentive Stock Option Grant Agreement under the 2008 Omnibus Incentive Plan, effective as of February 1, 2011, by and between the registrant and Brian M. Culley		Form 10-Q	001-32157-11823538	05/09/11

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10.21#	Amended and Restated 2008 Omnibus Incentive Plan	Form S-8	333-174940-11914946	06/16/11
10.22#	Form of Non-Statutory Stock Option Grant Agreement — Director under the Amended and Restated 2008 Omnibus Incentive Plan	Form S-8	333-174940-11914946	06/16/11
10.23#	Form of Incentive Stock Option Grant Agreement (for grants to the registrant's Chief Executive Officer and President and Chief Operating Officer made in July 2011) under the Amended and Restated 2008 Omnibus Incentive Plan	Form 10-Q	001-32157-111186142	11/08/11
10.24#	Form of Senior Executive Incentive Stock Option Grant Agreement (for grants to the registrant's Chief Executive Officer and President and Chief Operating Officer made beginning in December 2011) under the Amended and Restated 2008 Omnibus Incentive Plan	Form 10-K	001-32157-12677367	03/08/12
10.25#	2013 Omnibus Incentive Plan	Form 8-K	001-32157-13927320	06/21/13
10.26#	Form of Non-Statutory Stock Option Grant Agreement—Director (for grants to non-employee directors) under the 2013 Omnibus Incentive Plan	Form 8-K	001-32157-13927320	06/21/13
10.27#	Form of Incentive Stock Option Grant Agreement (for grants to employees) under the 2013 Omnibus Incentive Plan	Form 8-K	001-32157-13927320	06/21/13

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Exhibit No.	Description	Filed Herewith	Incorporated by Reference		Date Filed
			Form	File/Film No.	
10.28#	Form of Senior Executive Incentive Stock Option Grant Agreement (for grants to the registrant's chief executive officer and president and chief operating officer) under the 2013 Omnibus Incentive Plan		Form 8-K	001-32157-13927320	06/21/13
10.29#	2014 Omnibus Incentive Plan		Form 8-K	001-32157-14933081	06/20/14
10.30#	Form of Non-Statutory Stock Option Grant Agreement—Director (for grants to non-employee directors) under the 2014 Omnibus Incentive Plan		Form 8-K	001-32157-14933081	06/20/14
10.31#	Form of Incentive Stock Option Grant Agreement (for grants to employees) under the 2014 Omnibus Incentive Plan		Form 8-K	001-32157-14933081	06/20/14
10.32#	Form of Senior Executive Incentive Stock Option Grant Agreement (for grants to the registrant's chief executive officer and president and chief operating officer) under the 2014 Omnibus Incentive Plan		Form 8-K	001-32157-14933081	06/20/14
10.33#	Form of CMO Incentive Stock Option Grant Agreement (for grants to the registrant's chief medical officer) under the 2014 Omnibus Incentive Plan		Form 8-K	001-32157-14933081	06/20/14
10.34#	2015 Omnibus Incentive Plan		Form 8-K	001-32157-15934477	06/16/15
10.35#	Form of Non-Statutory Stock Option Grant Agreement—Director (for grants to non-employee directors) under the 2015 Omnibus Incentive Plan		Form 8-K	001-32157-15934477	06/16/15
10.36#				001-32157-15934477	06/16/15

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	Form of Incentive Stock Option Grant Agreement – Exempt Employees under the 2015 Omnibus Incentive Plan	Form 8-K
10.37#	Form of Incentive Stock Option Grant Agreement – Non-Exempt Employees under the 2015 Omnibus Incentive Plan	Form 001-32157-15934477 06/16/15 8-K
10.38#	Form of CEO Incentive Stock Option Grant Agreement under the 2015 Omnibus Incentive Plan	Form 001-32157-15934477 06/16/15 8-K
10.39#	Form of CMO Incentive Stock Option Grant Agreement under the 2015 Omnibus Incentive Plan	Form 001-32157-15934477 06/16/15 8-K
10.40#	Form of restricted stock units grant notice and agreement for awards approved on January 17, 2017	X
10.41#	Executive Severance Agreement, dated March 23, 2016, between the registrant and Brian M. Culley	Form 001-32157-161530105 03/25/16 8-K
10.42#	Executive Severance Agreement, dated March 23, 2016, between the registrant and Brandi L. Roberts	Form 001-32157-161530105 03/25/16 8-K
10.43#	Executive Severance Agreement, dated March 23, 2016, between the registrant and R. Martin Emanuele	Form 001-32157-161530105 03/25/16 8-K

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Exhibit No.	Description	Filed Herewith	Incorporated by Reference		Date Filed
			Form	File/Film No.	
10.44#	Executive Severance Agreement, dated March 23, 2016, between the registrant and Edwin L. Parsley		Form 10-Q	001-32157 161626040	05/06/16
10.45#	Executive Severance Agreement, dated March 23, 2016, between the registrant and Gregory D. Gorgas		Form 10-Q	001-32157 161626040	05/06/16
10.46#	Executive Severance Agreement, dated March 31, 2016, between the registrant and Shana Hood		Form 10-Q	001-32157 161626040	05/06/16
10.47#	2016 Executive Incentive Plan		Form 8-K	001-32157 161555255	04/05/16
10.48#	Separation Agreement and General Release of Claims between the registrant and R. Martin Emanuele, executed on October 31, 2016	X			
10.49#	Temporary Employment Agreement between the registrant and R. Martin Emanuele, executed on October 31, 2016	X			
10.50#	Separation Agreement and General Release of Claims between the registrant and Gregory D. Gorgas, executed on January 5, 2017	X			
10.51#	Director Compensation Policy, effective January 1, 2015		Form 10-K	001-32157- 15722085	03/24/15
10.52#	Form of Director and Officer Indemnification Agreement		Form 8-K	001-32157-061156993	10/23/06
10.53				001-32157-14949388	06/30/14

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	Sublease Agreement by and between the registrant and Santarus, Inc., effective as of June 19, 2014		Form 8-K
10.54	Form of Lock-Up Agreement, dated January 6, 2017		Form 001-32157-17515840 01/09/17 8-K
10.55	Form of Amendment No. 1 to Lock-Up Agreement, dated January 21, 2017		Form 001-32157-17510252 01/23/17 8-K
21.1	List of Subsidiaries	X	
23.1	Consent of Mayer Hoffman McCann P.C., Independent Registered Public Accounting Firm	X	
23.2	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm	X	
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a)	X	
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a)	X	
32.1±	Certification of principal executive officer and principal financial officer pursuant to 18 U.S.C. 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	X	
101.INS	XBRL Instance Document	X	

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Exhibit No.	Description	Filed Herewith	Incorporated by Reference	
			File/Film Form No.	Date Filed
101.SCH	XBRL Taxonomy Extension Schema Document	X		
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	X		
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document	X		
101.LAB	XBRL Taxonomy Extension Label Linkbase Document	X		
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document	X		

† Indicates that confidential treatment has been requested or granted to certain portions, which portions have been omitted and filed separately with the SEC

#Indicates management contract or compensatory plan

±These certifications are being furnished solely to accompany this report pursuant to 18 U.S.C. 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934 and are not to be incorporated by reference into any filing of the registrant, whether made before or after the date hereof, regardless of any general incorporation by reference language in such filing.