Savara Inc
Form 10-K
March 13, 2019

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2018

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO
Commission File Number 001-32157

Savara Inc.

(Exact name of Registrant as specified in its Charter)

Delaware (State or other jurisdiction of incorporation or organization)	84-1318182 (I.R.S. Employer Identification No.)
6836 Bee Cave Road, Building III, Suite 200 Austin, TX (Address of principal executive offices)	78746 (Zip Code)

Registrant’s telephone number, including area code: (512) 961-1891

Securities registered pursuant to Section 12(b) of the Act: Common Stock, Par Value $.001 Per Share; Common stock traded on The Nasdaq Global Select Market.

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 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 period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES NO

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). YES NO

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405) is not contained herein, and will not be contained, to the best of Registrant's knowledge, in definitive proxy or information statements 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, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	Accelerated filer
Non-accelerated filer	Smaller reporting company
	Emerging growth company

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on The Nasdaq Global Select Market on June 29, 2018, was $146,673,125.

The number of shares of Registrant's Common Stock outstanding as of March 13, 2019 was 35,336,438.

Portions of the Registrant's Definitive Proxy Statement relating to the Annual Meeting of Shareholders, scheduled to be held on May 29, 2019, are incorporated by reference into Part III of this Report.

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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,” “e “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:

- our plans, strategies and objectives for future operations, including the execution and timing of those plans;
- our future financial condition or performance, including the accuracy of our estimates regarding expenses, future revenues, capital requirements and needs for additional funding;
- the process and prospects for regulatory approval of our product candidates, including timing and outcomes of clinical studies;
- our beliefs regarding the therapeutic benefits of our product candidates;
- our beliefs regarding the treatment of conditions related to the indications targeted by our product candidates; and
- prospects for market success of our product candidates, including competition, intellectual property protection and infringement, third party payor coverage and reimbursement.

For a discussion of the factors that may cause our actual results, performance or achievements to differ materially from any future results, or performance or achievements expressed or implied in such forward-looking statements, see Part I, Item 1A, “Risk Factors,” in this report.

If any of these risks or uncertainties materialize 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 “Savara,” “our company,” “we,” “us,” “our,” or similar words refer to Savara Inc. together with its consolidated subsidiaries.

PART I

Item 1. Business.

Business Overview

Savara is an orphan lung disease company. Our current drug development pipeline comprises Molgradex, an inhaled granulocyte-macrophage colony-stimulating factor ("GM-CSF") in Phase 3 for autoimmune pulmonary alveolar proteinosis ("aPAP"), and in Phase 2a for nontuberculous mycobacterial ("NTM") lung infection and AeroVanc, a Phase 3-stage inhaled vancomycin for treatment of persistent methicillin-resistant Staphylococcus aureus ("MRSA") lung infection in individuals living with cystic fibrosis ("CF"). Our strategy involves expanding our pipeline of potentially best-in-class products through indication expansion, strategic development partnerships and product acquisitions, with the goal of becoming a leading company in the orphan lung disease market. Our management team has significant experience in orphan drug development and pulmonary medicine, identifying unmet needs, developing and acquiring new product candidates and effectively advancing them to approvals and commercialization.

The table below summarizes the current status and anticipated milestones for our primary drug development candidates.

Corporate Strategy

Our goal is to become a leader in orphan lung disease therapeutics through the development and commercialization of novel, best-in-class medicines that address unmet medical needs in this field. The key elements of our strategy include:

- Advance current pipeline. Advancing Savara's development pipeline is our highest priority. With Molgradex for aPAP and AeroVanc, we are focused on completing the current Phase 3 studies and, pending positive results, preparing to submit a Biologics License Application ("BLA") and New Drug Application ("NDA"), respectively, to the U.S. Food and Drug Administration (the "FDA"), ensuring our product supply chains will support commercialization, and preparing for potential commercialization of Molgradex and AeroVanc in the U.S., throughout Europe, Japan and other countries. Regarding Molgradex for NTM, our focus is on the completion of the current Phase 2a study and, pending positive results, preparing for and executing a well-controlled Phase 2b study.

- Pursue Molgradex and AeroVanc indication expansion. While our immediate priority is to obtain regulatory approvals in the primary indications described above, we are exploring the utility of Molgradex and AeroVanc in other difficult-to-treat lung infections.

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Expand the product pipeline through strategic product acquisitions. Concurrent with our indication expansion efforts, our strategy includes growing our development pipeline through strategic partnerships and product acquisitions. A key priority has been to enhance the delivery of known chemical entities or drug classes, e.g., changing the route of delivery of a drug directly into the lungs, for the treatment of serious or life-threatening lung diseases. While we have developed an internal core competence in inhaled drug development, we are technology and route-of-delivery agnostic. Future product acquisition decisions will be based on the unmet medical need within a specific disease, the market opportunity and the ability to rapidly develop and commercialize a product candidate.

- Outsource capital intensive operations. We will continue to pursue the development and manufacturing of our product candidates by outsourcing most clinical development and all manufacturing operations. We believe our business model has facilitated effective development of our pipeline by using high quality specialist vendors and consultants in a capital efficient manner.

- Establish internal sales and marketing capabilities to commercialize our products in the U.S. & EU. Pending FDA approval, we plan to commercialize our products through an internal specialty sales force in the U.S. Pending European Medicines Agency ("EMA") approval, we expect to commercialize Molgradex and AeroVanc in certain key markets in the EU and may engage with strategic partners to optimize sales and promotion activities in the remaining EU territories.

Molgradex – aPAP

Our lead product candidate, Molgradex, an inhaled formulation of recombinant human GM-CSF, is being developed for the treatment of autoimmune pulmonary alveolar proteinosis ("aPAP"). Pulmonary alveolar proteinosis ("PAP") is a rare lung disease characterized by the build-up of lung surfactant in the alveoli (or air sacs) of the lungs. There are different types of PAP, of which aPAP is the most common.

Molgradex is currently being investigated in a pivotal Phase 3 clinical study, called IMPALA, for the treatment of aPAP. Molgradex has been granted Orphan Drug Designation for the treatment of aPAP in the U.S. and the EU, which allows for seven and ten years of exclusivity from approval, respectively. In addition, Savara has exclusive access to the PARI Investigational eFlow Nebulizer System for this indication along with a proprietary cell bank for molgramostim, an inhaled, non-glycosylated form of GM-CSF and the active drug substance of Molgradex.

There are approximately 2,200 PAP patients in the U.S., with the vast majority having aPAP. The disease process underlying aPAP involves an autoimmune response against GM-CSF, a naturally occurring protein that functions to clear excess surfactant from the alveoli. The autoimmune response suppresses the stimulating activity of GM-CSF on lung macrophages, resulting in the accumulation of excess surfactant. The surfactant consists of proteins and lipids and is an important physiological substance that lines the inside of the alveoli to prevent the lungs from collapsing. In a healthy lung, the old and inactivated surfactant is cleared and digested by immune cells called alveolar macrophages. Alveolar macrophages need to be stimulated by GM-CSF to function properly in clearing surfactant. In aPAP, GM-CSF is neutralized by antibodies against GM-CSF, rendering the macrophages unable to perform their tasks. As a result, an excess of surfactant accumulates in the alveoli, obstructs gas exchange, and results in shortness of breath and decreased exercise tolerance. Patients may also experience chronic cough, as well as episodes of fever, chest pain, or coughing blood, especially if secondary lung infection develops. In the long term, the disease can lead to serious complications, including lung fibrosis and the need for a lung transplant. There are no currently approved therapies for the treatment of aPAP. The current standard-of-care is a surgical procedure called whole lung lavage ("WLL"), which entails washing out the lungs bronchoscopically with saline, segment-by-segment, under general anesthesia. By nature, WLL is an invasive and inconvenient procedure that requires highly experienced physicians and hospitalization at specialist sites. Based on published investigator-sponsored treatment experience with inhaled GM-CSF, we believe Molgradex has the potential to replace the inactivated GM-CSF in aPAP patients, thereby restoring the surfactant clearing activity of the alveolar macrophages, and become the first-line treatment-of-choice for aPAP.

The pivotal Phase 3 IMPALA clinical study is being conducted in 18 countries including the U.S., Japan, and throughout Europe. IMPALA is a randomized, double-blind, placebo-controlled study designed to compare the efficacy and safety of Molgradex with placebo in patients with aPAP. In 2017, we announced our expedited U.S. development strategy for Molgradex, which enables the ongoing IMPALA study to serve as a pivotal study also for U.S. registration purposes. In support of this strategy, we submitted an Investigational New Drug ("IND") application to the FDA in December 2017 to expand the study into U.S. sites. The primary endpoint of the study is the alveolar-arterial oxygen gradient, or (A-a)DO_2, a commonly used measure of oxygenation impairment. In addition, the FDA will focus its review on three key secondary endpoints that will be assessed to show improvement in clinical symptoms and function. Patients are randomized to receive treatment for up to 24 weeks in one of three treatment arms: 1) Molgradex 300 µg administered once daily, 2) Molgradex 300 µg and matching placebo administered daily in 7-day intermittent cycles of each, or 3) inhaled placebo administered once daily. Patient enrollment was completed for IMPALA in October 2018 with a total of 139 patients. Topline results are expected at the end of Q2 2019.

In March 2018, we initiated the IMPALA-X study. This open-label extension study allows patients who are rolling off IMPALA to continue treatment for up to three additional years and will determine the long-term safety and utilization of Molgradex in patients with aPAP. Active enrollment in this study continues.

Molgradex - NTM

Molgradex is also being investigated for the treatment of NTM lung infection in an open-label, non-controlled Phase 2a study called OPTIMA. NTM lung infection is a rare and serious lung disorder associated with increased rates of morbidity and mortality. Nontuberculous mycobacteria are naturally-occurring organisms, and NTM lung infection can occur when the organism (found in the environment) is inhaled and an individual develops a slowly progressive and destructive lung disease. NTM lung infection is typically characterized by cough, fatigue, and weight loss. NTM infections often become chronic and require long courses of multiple antibiotics, and despite aggressive treatment regimens, treatment failure rates are high and recurrence of infection common. Chronic NTM lung infection can have a significant impact on quality of life. There are up to 80,000 individuals affected in the U.S., and the most common types of NTM lung infection involve Mycobacterium avium complex ("MAC"), and Mycobacterium abscessus ("MABSC"). There have been few advancements in new systemic treatments for NTM lung infection.

NTM lung infections are a considerable therapeutic challenge due to the unique ability of these bacteria to evade the normal killing mechanisms of alveolar macrophages, a type of immune cell responsible for killing bacteria in the lungs. There is increasing scientific literature suggesting that GM-CSF plays an important role in enhancing the ability of macrophages to clear mycobacteria.[1] For instance, GM-CSF knock out mice inoculated with MABSC develop a chronic lung disease resembling human chronic infection, whereas wild type mice with intact GM-CSF production typically clear the bacteria quickly and fail to develop chronic infection. In animal studies, GM-CSF has been shown to kill NTM with similar efficacy compared to commonly used NTM antibiotics, and the simultaneous use of GM-CSF with antibiotics can further improve the antibacterial effect of either GM-CSF or antibiotics given alone.

In two published clinical case reports in the European Respiratory Journal by Dr. Wylam of the Mayo Clinic,[2] inhaled GM-CSF was shown to eradicate or dramatically reduce the bacterial burden in patients with chronic MABSC lung infection. This suggests that the promising animal data may be translatable to humans, and the potential therapeutic role of GM-CSF in NTM lung infection warrants more intensive investigation.

The multi-center OPTIMA study in non-CF patients was initiated in Q1 2018 and is investigating the efficacy of Molgradex on reduction of NTM bacterial load in sputum, NTM sputum culture conversion to negative, exercise capacity, patient reported outcomes and safety. Two groups of patients were recruited for the study - those on anti-mycobacterial treatment and those not on anti-mycobacterial treatment. Both groups receive Molgradex 300 µg administered once daily. The primary endpoint is sputum culture conversion during the treatment period, defined as at least three consecutive negative sputum samples. Interim results from the OPTIMA study were disclosed in December 2018. Based on the microbiological data and safety profile, which provides the basis to continue treating patients for a longer period of time, the duration of the OPTIMA study was extended from 24 to 48 weeks, with a 12-week follow up period at the end of treatment. This increases the ability to observe a more robust anti-infective effect, including culture conversions. Final results from the study are expected in the first quarter of 2020.

In Q3 2018, the IND application for Molgradex in CF-affected patients with chronic NTM lung infection was accepted by the FDA. A Phase 2a study of Molgradex in CF-affected patients with NTM lung infection is expected to initiate in Q1 2019.

AeroVanc

Our second Phase 3 product candidate, AeroVanc, is a vancomycin hydrochloride inhalation powder. AeroVanc is the first inhaled antibiotic in development for the treatment of persistent MRSA lung infection in individuals living with CF. AeroVanc was granted Orphan Drug Designation and Qualified Infectious Disease Product ("QIDP") status for the treatment of persistent MRSA lung infection in individuals living with CF in the U.S. Orphan Drug Designation makes AeroVanc eligible for seven years of exclusivity from approval in the U.S., and the QIDP designation makes AeroVanc eligible for an additional five years of exclusivity in the U.S. In 2017, a composition of matter patent covering AeroVanc was issued by the U.S. Patent and Trademark Office ("USPTO"), which affords us important protection for the program in the largest market for the product (the U.S.), augments our market protection strategy and will not expire earlier than 2032.

[1] deSilva T.I., et al. Journal of Infection (2007) 54 (e207-e210); Hallstrand T.S., et al. European Respiratory Journal (2004) 24 (367-370); Groote et al, J Antimicrob Chemother. 2014 Apr;69(4):1057-64.; Luiz E. Bermudez, et al. The Journal of Infectious Diseases, Volume 169, Issue 3, 1 March 1994, Pages 575–580.

[2] Scott et al, European Respiratory Journal (2018) (DOI: 10.1183/13993003.02127-2017).

CF is a genetic disease that involves sticky mucus buildup in the lungs, persistent lung infections and permanent and progressive respiratory disability. There are approximately 30,000 individuals affected by CF in the U.S., and MRSA infection has become increasingly common in people living with CF, with a prevalence of approximately 26%. Persistent MRSA infection in people living with CF is associated with increased use of intravenous ("IV") antibiotics, increased hospitalizations, a more rapid rate of decline in lung function, and shortened life-expectancy. Due to the lung pathology associated with CF, persistent MRSA lung infection is difficult to eradicate or manage using oral or IV antibiotics, and there is currently no standard-of-care to manage this condition. Whereas inhaled antibiotics have become a cornerstone of treating the most prevalent chronic pathogen in individuals living with CF, Pseudomonas aeruginosa ("Pseudomonas"), there are no approved inhaled antibiotics addressing MRSA lung infection. In a randomized, double-blind, placebo-controlled Phase 2 study in individuals living with CF with persistent MRSA infection, AeroVanc met a primary endpoint to reduce MRSA density in sputum, and showed encouraging trends of improvement in lung function and respiratory symptoms, as well as prolongation of the time-to-use of other antibiotics, with best responses in patients under 21 years of age.

AeroVanc is currently being investigated in a pivotal Phase 3 clinical study, called AVAIL, in the U.S. and Canada for the treatment of persistent MRSA lung infection in individuals living with CF. The study began enrolling patients at U.S. and Canadian clinical sites in September 2017 and December 2017, respectively. The study is expected to enroll approximately 200 patients (150 patients ≤ 21 years old, 50 patients > 21 years old). During Period 1 of the study, patients are randomly assigned in a blinded 1:1 fashion to receive either AeroVanc (30 mg) twice daily, or placebo, by inhalation for 24 weeks or 3 dosing cycles. A dosing cycle is defined as 28 days of treatment followed by 28 days of observation. During Period 2 of the study, patients receive open-label AeroVanc (30 mg) twice daily for an additional 24 weeks or 3 dosing cycles, to evaluate the long-term safety of AeroVanc. The primary endpoint is the mean absolute change in Forced Expiratory Volume in the first second ("FEV1") percent predicted from baseline, which will be analyzed sequentially at week 4 (the end of cycle 1), week 12 (the end of cycle 2), and at week 20 (the end of cycle 3). Analysis of the primary endpoint will be based on patients 6 21 years of age. Secondary endpoints include: (i) time-to-use of another antibiotic medication (oral, IV, and/or inhaled) for pulmonary infection, (ii) the number of successful FEV1-response cycles a patient achieves over Period 1 (weeks 4, 12, and 20), (iii) relative change from baseline in FEV1 percent predicted at weeks 4, 12, and 20, (iv) change from baseline Cystic Fibrosis Questionnaire-Revised scores at weeks 4, 12, and 20 and (v) change from Baseline in Cystic Fibrosis Respiratory Symptom Diary-Chronic Respiratory Symptom Score at weeks 4, 12, and 20. We anticipate that AVAIL patient enrollment will be completed in Q3 2019, with top line results expected in Q2 of 2020.

Detailed Program Descriptions

Molgradex

Background on aPAP

PAP is a rare lung disease, which affects up to seven out of a million people in the U.S.[3], and has a similar prevalence in Japan[4]. PAP is characterized by the build-up of lung surfactant in the alveoli, or air sacs, of the lungs. The surfactant consists of proteins and lipids and is an important physiological substance that coats the inside of the alveoli

to prevent the lungs from collapsing. The lungs continuously produce new active surfactant. In a healthy lung, the old and inactivated surfactant is cleared and digested by immune cells called alveolar macrophages. However, in lungs of patients with aPAP, the macrophages fail to clear the surfactant from the alveoli, leading to gradual accumulation of excess surfactant in the alveoli. The root cause of aPAP is an autoimmune response against a naturally occurring protein in the body, GM-CSF. Pulmonary macrophages need to be stimulated by GM-CSF to function properly, but in aPAP, GM-CSF is deactivated by antibodies against GM-CSF, rendering the macrophages unable to perform their tasks, such as clearing the surfactant from the alveoli.

aPAP most commonly affects men in early middle age, but both sexes and patients of any age can be affected. As a result of the accumulation of excess surfactant, gas exchange in the lungs is obstructed, and patients start to experience shortness of breath, and decreased exercise tolerance. Shortness of breath is typically first observed upon exertion, but as the disease progresses, also at rest. Patients may experience chronic cough, as well as episodes of fever, chest pain, or coughing blood, especially if secondary lung infection develops. In the long term, the disease can lead to serious complications, including lung fibrosis and the need for lung transplant. Mortality due to aPAP has decreased over the last decades with better clinical management, but in rare cases serious lung infections or respiratory insufficiency may lead to death.

[3] Trapnell BC, Avetisyan R, Carey B, Zhang W, Kaplan P, Wang H. Prevalence of pulmonary alveolar proteinosis (PAP) determined using a large health care claims database. Am J Respir Crit Care Med. 2014;VOL:abstract A6582.

[4] Inoue Y, Trapnell BC, Tazawa R, Arai T, Takada T, Hizawa N et al. Characteristics of a large cohort of patients with autoimmune pulmonary alveolar proteinosis in Japan. Am J Respir Crit Care Med 177: 752–62, 2008.

Current treatment options for aPAP

The current standard-of-care for aPAP is a surgical procedure called Whole Lung Lavage ("WLL"), which entails washing out the lungs with saline under general anesthesia. WLL is an invasive and inconvenient procedure that requires highly experienced physicians at specialist sites. The procedure is conducted in an operating room, requiring hospitalization and admission to intensive care after the procedure. In many patients, WLL only provides temporary symptomatic relief, and once the lungs refill with surfactant, the WLL procedure needs to be repeated.

As there are no approved drug treatments available for aPAP, we believe there is a high need for a convenient and efficacious medicinal treatment. We believe that inhalation of GM-CSF directly into the lungs has the potential to replace the inactivated GM-CSF, and thereby restore the surfactant clearing activity of the alveolar macrophages. As a result, we believe that inhaled GM-CSF has the potential for considerable improvement in oxygenation and exercise tolerance. An injectable form of GM-CSF, sargramostim, is approved and on the market in the U.S. for IV and subcutaneous administration for the treatment of neutropenia caused by cancer chemotherapy, but there is currently no approved inhalation formulation of GM-CSF.

The potential benefits of inhaled GM-CSF in aPAP, together with the availability of sargramostim, have stimulated independent clinicians and academic researchers in the U.S., Europe, and Japan to study the safety and efficacy of GM-CSF, administered by inhalation, in aPAP patients. Several such investigator-sponsored, open-label clinical studies and case studies of inhaled GM-CSF treatment have been published, with promising results on the efficacy and safety of the treatment.[5,6,7] In total, treatment of more than 80 aPAP patients with inhaled GM-CSF has been reported in open-label studies or retrospective cohorts, as well as several individual case reports. Whereas the majority of the patients described in the literature received sargramostim, the results indicate that both sargramostim and molgramostim have the potential for a positive impact on oxygenation and clinical symptoms in aPAP patients.

According to our review of published literature, few safety issues related with molgramostim or sargramostim inhalation in patients with aPAP have been reported. However, there is still limited information available on the long-term safety of inhaled GM-CSF. In indications other than aPAP, more than 100 patients, mainly with a cancer diagnosis, have received inhaled sargramostim, in doses up to 4000 µg/day. Pulmonary toxicity was the most frequently reported toxicity at high doses. An increase in both number and severity of adverse events with increasing dose has been observed. However, due to the underlying diseases it was often difficult for the investigators to assess causality of the adverse event cases.

Molgradex Product Description

Molgradex is a novel inhaled formulation of recombinant human GM-CSF being developed for the treatment of aPAP. The active drug substance, molgramostim, is a non-glycosylated form of GM-CSF. GM-CSF is an endogenous growth factor that stimulates the proliferation and differentiation of hematopoietic cells (blood and immune cells), mainly granulocytic and monocytic cell lines, which serve as the body's first line of defense against bacteria and viruses, and

also function to clear cellular debris and waste substances from the body. Molgramostim is produced in a strain of Escherichia coli bearing a genetically engineered plasmid containing a human GM-CSF gene.

Molgradex, is a sterile nebulizer solution in a vial containing 300 µg of molgramostim, designed to be administered once daily by inhalation via a high efficiency Investigational eFlow Nebulizer System (PARI Pharma GmbH, Germany). The PARI eFlow Nebulizer system for use with investigational drug products is a reusable electronic inhalation system that has been optimized for administration of Molgradex.

Molgradex was granted Orphan Drug Designation by the FDA in October 2012, and by the EMA in July 2013, for the treatment of aPAP. Since 2014, Molgradex has been available in several European countries for the treatment of aPAP for named patients following unsolicited physician requests.

[5] Tazawa R, Trapnell BC, Inoue Y, Arai T, Takada T, Nasuhara Y, et al. Inhaled Granulocyte/Macrophage–Colony Stimulating Factor as Therapy for Pulmonary Alveolar Proteinosis. Am J Resp Crit Care Med 181: 1345-1354, 2010.

[6] Wylam ME, Ten R, Prakash UB, Nadrous HF, Clawson ML and Anderson PM (2006). Aerosol granulocyte-macrophage colony-stimulating factor for pulmonary alveolar proteinosis. Eur Respir J 27(3): 585-93.

[7] Papiris SA, Tsirigotis P, Kolilekas L, Papadaki G, Papaioannou AI, Triantafillidou C, et al. (2014). Long-term inhaled granulocyte macrophage-colony-stimulating factor in autoimmune pulmonary alveolar proteinosis: effectiveness, safety, and lowest effective dose. Clin Drug Investig 34(8): 553-64.

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We anticipate that Molgradex will be used as a long-term therapy in patients with aPAP. The optimal duration of treatment is currently not known, and is likely to vary between patients depending on the disease severity and the natural course of their disease. Molgradex treatment may not entirely eliminate the need for WLL in all patients, but based on interviews conducted by us, PAP centers that have experimented with long-term inhaled GM-CSF have seen a considerable reduction of WLL procedures.

Molgradex Key Advantages

Building upon the published investigator-sponsored treatment experience with inhaled GM-CSF, we believe Molgradex has the potential to become the treatment of choice for aPAP. Molgradex has the following characteristics that we believe will contribute to the clinical profile of the product candidate, as well as facilitate our regulatory approval and successful commercialization.

Specifically, Molgradex offers:

- Strong product foundation, applying a previously approved active drug substance class and previously approved drug delivery technology.

- GM-CSF delivery directly to the lungs, the primary site of macrophage function deficiency, which we believe can result in high clinical efficacy with limited systemic adverse effects.

- High efficiency nebulizer providing a fast and convenient method of administration, which is highly desirable for long-term treatment in a chronic disease, such as aPAP.

- Eligibility for strong market protection via orphan drug status, a proprietary cell bank used in the production of the drug substance, and an exclusive device supply agreement.

Clinical Development of Molgradex aPAP

Ongoing Phase 3 IMPALA Study

We are currently conducting a pivotal Phase 3 clinical study of Molgradex, called IMPALA, in 18 countries including the U.S., Japan, and throughout Europe. IMPALA is a randomized, double-blind, placebo-controlled study designed to compare the efficacy and safety of Molgradex with placebo in patients with aPAP. The study began enrolling patients in Europe and Japan in 2016. In 2017, we announced our expedited U.S. development strategy for Molgradex, which enables the ongoing IMPALA study to serve as a pivotal study for U.S. registration purposes. In support of this strategy, we submitted an IND application to the FDA in December 2017 to expand the study into U.S. sites. The primary endpoint of the study is (A-a)DO_2, a commonly used measure of oxygenation impairment. IMPALA is over 90% powered to detect a 10mmHg change in (A-a)DO_2 from baseline versus placebo. In addition, the FDA will focus

its review on three key secondary endpoints that will be assessed to show improvement in clinical symptoms and function. To help ensure adequate statistical power by confirming or modifying the study sample size, the IND submission included a blinded interim check of the variability of two of the key secondary endpoints - the six-minute walk distance and St. George's respiratory questionnaire. This blinded analysis indicated that the original sample size of 90 patients was sufficient to achieve 90% power for one of the two secondary endpoints. However, to achieve 90% power for both secondary endpoints, and thereby further increase the likelihood of a robust and convincing study outcome, the sample size was increased to a total of 135 patients, or 45 patients per treatment arm. Patients are randomized to receive treatment for up to 24 weeks in one of three treatment arms: 1) Molgradex 300 µg administered once daily, 2) Molgradex 300 µg and matching placebo administered daily in 7-day intermittent cycles of each, or 3) inhaled placebo administered once daily. At the end of the 24-week double-blind period, all treatment arms roll into a 24-week open-label follow up period and receive Molgradex 300 ug administered daily in 7-day intermittent cycles.

Patient enrollment in IMPALA is complete, and we anticipate top line results at the end of Q2 2019.

In March 2018 we initiated the IMPALA-X study. This open-label extension study allows patients who are rolling off IMPALA to continue treatment for up to three additional years and will determine the long-term safety and utilization of Molgradex in patients with aPAP. Active enrollment in this study continues.

Completed Phase 1 Clinical Study

In a Phase 1 study evaluating the safety and tolerability of Molgradex in 42 healthy adult volunteers, the drug was generally well tolerated and produced dose-dependent increases in total and differential white blood cell counts consistent with the known pharmacologic effect of GM-CSF. The study was a randomized, double-blind, placebo-controlled, single ascending dose ("SAD") and multiple ascending dose ("MAD") study to assess the safety, tolerability, pharmacokinetics, and pharmacodynamics of Molgradex. As part of the SAD arm, 18 subjects were included with four subjects randomized to each of the three SAD dose levels (150 µg, 300 µg and 600 µg) and six subjects received placebo for a duration of six days. As part of the MAD arm, 24 subjects were included with nine subjects randomized to each of the two MAD dose levels (300 µg or 600 µg) and six subjects received placebo for a duration of six days.

In the SAD arm, GM-CSF was absorbed into the systemic circulation with a time to reach peak serum concentration ("Tmax") of two hours after inhalation of Molgradex; however, at picogram levels, 50 to 100 times lower than what has been observed following similar doses of IV-administered GM-CSF. Total systemic exposure (AUC last) increased with dose, ranging between 13 and 138 pg•h/mL and maximum concentration ("Cmax") ranging between 9.1 and 41 pg/mL (Cmax was similar for the 300 and 600 µg dose levels). In the MAD arm, there was evidence of some accumulation after multiple dosing; Cmax increased from 32 pg/mL on Day 1 to 90 pg/mL on Day 6 at the 300 µg dose level, and from 96 pg/mL on Day 1 to 251 pg/mL on Day 6 at the 600 µg dose level. Likewise, AUC last increased from 97 to 248 pg•h/mL from Days 1 to 6 for the 300 µg dose level and from 350 to 802 pg•h/mL for the 600 µg dose level. Minimum measurable plasma concentrations ("Cmin") on Day 6 were 3.6 and 5.1 pg/mL measured at 8 and 12 hours, respectively for the 300 µg and 600 µg dose levels. In subjects treated with Molgradex, a slight increase in total white blood cell and differential counts (primarily within normal reference ranges) was observed in a dose-dependent manner, in-line with the known biological mode-of-action of GM-CSF.

No meaningful difference in the frequency or severity of adverse events was observed between Molgradex 300 µg and placebo. The most common adverse event was cough, reported in 21 out of 30 subjects (70%) receiving Molgradex and 8 out of 12 subjects (67%) receiving placebo, and there was no difference in the causality assessment between the treatment arms. A higher number of treatment-related adverse events were observed at the 600 µg dose compared to the 300 µg dose and placebo in the MAD arm. There were no serious or severe adverse events, dose-limiting toxicity or other remarkable findings of clinical concern in the safety data.

Background on NTM

NTM lung infection is a rare and serious lung disorder associated with increased rates of morbidity and mortality. Nontuberculous mycobacteria are naturally occurring organisms and NTM lung infection can occur when an individual inhales the organism from their environment and develops a slowly progressive and destructive lung disease. NTM lung infection is typically characterized by cough, fatigue, and weight loss. NTM infections often become chronic and require long courses of multiple antibiotics, and despite aggressive treatment regimens, treatment failure rates are high, and recurrence of infection common. Chronic NTM lung infection can have a significant impact on quality of life. There are up to 80,000 individuals affected in the U.S, and the most common types of NTM lung infection involve MAC and MABSC. There have been few advancements in new systemic treatments for NTM lung infection. However, in a 2017 Phase 3 clinical study, local delivery of an inhaled form of amikacin directly to the lung was shown to be effective in approximately one third of treatment refractory patients with pulmonary MAC infection. This suggests that administration of high local concentrations of drug directly at the site of infection provides an attractive new avenue to improve clinical outcomes in this and other difficult-to-treat chronic lung infections.

NTM lung infections are a considerable therapeutic challenge due to the unique ability of these bacteria to evade the normal killing mechanisms of alveolar macrophages, a type of immune cells responsible for killing bacteria in the lungs. There is increasing scientific literature suggesting that GM-CSF plays an important role in enhancing the ability of macrophages to clear mycobacteria.[8] For instance, GM-CSF knock out mice inoculated with MABSC develop a chronic lung disease resembling human chronic infection, whereas wild type mice with intact GM-CSF production typically clear the bacteria quickly and fail to develop chronic infection. In animal studies, GM-CSF has been shown to kill NTM with similar efficacy compared to commonly used NTM antibiotics, and the simultaneous use of GM-CSF with antibiotics can further improve the antibacterial effect of either GM-CSF or antibiotics given alone.

In two published clinical case reports in the European Respiratory Journal by Dr. Wylam of the Mayo Clinic,[9] inhaled GM-CSF was shown to eradicate or dramatically reduce the bacterial burden in patients with refractory MABSC lung infection. This suggests that the promising animal data may be translatable to humans, and the potential therapeutic role of GM-CSF in NTM lung infection warrants more intensive investigation. Among the various NTM species, MABSC is a particularly challenging clinical problem, as it is one of the most resistant organisms to antibiotics. Importantly, GM-CSF is not an antibiotic that targets the bacteria. Rather, it is an anti-infective immunotherapy that targets the human immune response, not the bacteria directly, thus avoiding the increasing problem of antibiotic resistance.

Clinical Development of Molgradex NTM

A Phase 2a multi-center clinical study in non-CF patients, called OPTIMA, was initiated in Q1 2018 and is investigating the efficacy of Molgradex on reduction of NTM bacterial load in sputum, NTM sputum culture conversion to negative, exercise capacity, patient reported outcomes and safety.

[8] deSilva T.I., et al. Journal of Infection (2007) 54 (e207-e210); Hallstrand T.S., et al. European Respiratory Journal (2004) 24 (367-370); Groote et al, J Antimicrob Chemother. 2014 Apr;69(4):1057-64.; Luiz E. Bermudez, et al. The Journal of Infectious Diseases, Volume 169, Issue 3, 1 March 1994, Pages 575–580.

[9] Scott et al, European Respiratory Journal (2018) (DOI: 10.1183/13993003.02127-2017).

OPTIMA is an open-label, non-controlled, multi-center, Phase 2a clinical study of Molgradex in 32 subjects (≥18 years of age) with persistent NTM lung infection. OPTIMA enrolled subjects with chronic MAC or MABSC infection, with all patients having either antibiotic refractory infection or intolerance to standard NTM antibiotics. The study initially consisted of a 24-week treatment period and a 12-week follow up period. Two groups of subjects were recruited into the OPTIMA study. Group 1 consists of patients who remained sputum culture positive while currently on a multidrug NTM guideline-based anti-mycobacterial regimen, which had been ongoing for at least six-months prior to the baseline visit. Group 2 consists of patients who remained sputum culture positive, but either stopped a multidrug NTM guideline-based anti-mycobacterial regimen at least 28 days prior to screening due to lack of response or intolerance, or never started such treatment.

The primary endpoint in the study is sputum culture conversion, defined as at least three consecutive sputum samples without growth of NTM. Secondary endpoints include: (i) the number of patients with sputum smear conversion to negative, defined as at least three consecutive negative acid-fast bacilli ("AFB") stained sputum smears on microscopy among patients who were smear positive at baseline, (ii) the number of patients with durable sputum culture conversion, defined as sputum culture conversion at or before week 48 and culture still negative for growth of NTM at 12-week follow up, (iii) the number of patients with durable sputum smear conversion, defined as sputum smear conversion at or before week 48 and AFB stained smear still negative for NTM at 12-week follow up among patients who were smear positive at baseline, and (iv) other microbiological indicators, exercise capacities and patient reported outcomes.

Interim results from the OPTIMA study were disclosed in December 2018.

The interim analysis focused on efficacy, as assessed by microbiological results, in 14 patients who completed the 24-week treatment period and had culture results available up to at least the 16-week timepoint. Ten of the evaluable patients have MAC infection and four have MABSC infection. Of the patients with MAC infection, eight are in treatment Group 1 (on anti-mycobacterial treatment) and two are in treatment Group 2 (not on anti-mycobacterial treatment). The four evaluable MABSC patients are evenly split between both treatment groups. Safety and tolerability was assessed for all 32 patients enrolled in the study.

The data show that among the 10 patients with MAC infection, four experienced a consistent sputum smear conversion to negative by week 24, and three experienced a negative sputum culture at weeks 16 and 20, with culture results pending for the week 24 timepoint. Sputum smear or sputum culture conversions were not observed in the four patients with MABSC infection. Due to the generally slow growth of NTM on culture media, a sputum sample can be determined negative only after eight weeks of observation, causing a corresponding lag time in the assessment of the culture data.

Safety was assessed in the total study population. Among the 32 patients, six (19%) experienced serious adverse events ("SAEs"), including one patient who died by suicide. The death was considered unrelated to treatment. The majority of SAEs consisted of hospitalizations due to pulmonary exacerbations or worsening of NTM infection, of

which one was considered possibly treatment-related. GM-CSF was generally well tolerated, with nine patients (28%) reporting mostly mild, potentially treatment-related respiratory adverse events. Respiratory adverse events were defined as shortness of breath, chest tightness or wheeze. A total of three patients (9%) discontinued treatment due to adverse events.

Consistent with the systemic pharmacological effect of GM-CSF on white blood cells, 17 patients (53%) experienced increased levels of blood eosinophils. The increase generally peaked at the week 4 timepoint, and levels decreased or plateaued at subsequent visits.

Based on the microbiological data and safety profile, which provides the basis to continue treating patients for a longer period of time, the duration of the OPTIMA study was extended from 24 to 48 weeks, with a 12-week follow up period at the end of treatment. This increases the ability to observe a more robust anti-infective effect, including culture conversions. The primary endpoint is sputum culture conversion during the treatment period, defined as at least three consecutive negative sputum samples. Final results from the study are expected in the first quarter of 2020.

In Q3 2018, the IND application for Molgradex in CF-affected patients with chronic NTM lung infection was accepted by the FDA. A Phase 2a study of Molgradex in CF-affected individuals with NTM lung infection is expected to initiate in Q1 2019.

Overview of AeroVanc

Background on MRSA Infection in CF

CF is a genetic disease characterized, in part, by the prevalence of thick, sticky mucus produced in the lung, frequent lung infections, and a resultant decline in pulmonary function. As the disease progresses, patients' lungs are typically infected with bacteria that are difficult to eradicate. Inhaled antibiotics have become a cornerstone for the treatment of the most common chronic pathogen, Pseudomonas, in order to control the infection and improve lung function and quality of life. In recent years, MRSA lung infection has become increasingly common in CF, with a prevalence of 26% according to the most recent (2017) data report of the Cystic Fibrosis Foundation. Importantly, persistent MRSA lung infection has been associated with worse clinical outcomes in CF, including a more rapid rate of decline in lung function[10] and a shorter life expectancy.[11] The increasing prevalence and high clinical impact of MRSA infection in CF have resulted in an unmet need for improved therapies to help address the condition. Considering the established practice of treating chronic Pseudomonas infection in CF using inhaled antibiotics, all of which have limited activity against MRSA, it would be logical to attempt treatment of chronic MRSA infection with an inhaled antibiotic that is active against MRSA. We believe that AeroVanc is the first inhaled antibiotic being developed to specifically treat MRSA infection of the lungs.

Current MRSA treatment options in CF

Persistent MRSA lung infection in people living with CF is difficult to eradicate or manage using oral or IV antibiotics. Currently, there is no standard of care to manage the infection despite the high need.[12] In contrast to the established treatment of Pseudomonas infection with inhaled antibiotics, there is no FDA-approved inhaled antibiotic treatment available for MRSA infection.

For people living with CF who have MRSA infection, IV vancomycin or linezolid are the most commonly used drugs for the treatment of acute pulmonary exacerbation, and these drugs may be used in combination with other IV antibiotics in patients with simultaneous Gram-negative infections, such as Pseudomonas. For MRSA lung infection, vancomycin is available exclusively in IV form, and while highly effective against MRSA and other Gram-positive bacteria, chronic home-based use of IV vancomycin is not practical, and chronic use has also been associated with systemic toxicity, especially renal toxicity and ototoxicity.

According to our research, there is increasing clinical need to treat chronic MRSA infection in CF. In the absence of an inhaled antibiotic, there is emerging use of oral anti-MRSA antibiotics in an attempt to suppress the MRSA infection and reduce the occurrence of acute pulmonary exacerbations. According to our survey results, 27% of the surveyed CF specialists in the U.S. regularly use antibiotics targeting MRSA as a suppressive treatment (any dosage form) in patients with frequent exacerbations or other symptoms for which MRSA is considered a cause or contributing factor. This practice is emerging despite the absence of established consensus or guidelines relating to the use of oral anti-MRSA antibiotics in CF, or evidence of efficacy established in controlled studies.

As with current inhaled anti-pseudomonal drugs, we believe that there is significant clinical advantage in delivering an anti-MRSA antibiotic, such as vancomycin, directly to the site of infection to maximize the clinical efficacy, reduce systemic exposure and the risk of adverse effects, and to enable convenient use of the product outside of the hospital setting. The aerosolized IV form of vancomycin, administered by nebulization, has been used in multiple small published clinical studies, mainly to treat ventilator-associated pneumonia in an intensive care setting. In these studies and case reports, nebulized vancomycin had good antibacterial efficacy and was generally well tolerated. According to our research, in recent years many of the leading CF centers in the U.S. have explored the use of inhaled vancomycin to treat MRSA on a chronic basis, by nebulizing the IV form of vancomycin. The experience gained from this type of treatment has been encouraging and provides anecdotal reports of the safety and clinical utility of inhaled vancomycin for a period of several years in some patients. Similarly, in the 1990's, nebulized IV tobramycin was explored as a treatment of Pseudomonas infections in people living with CF. This exploration resulted in the development of the most widely used inhaled antibiotic worldwide, and is a cornerstone of chronic treatment of Pseudomonas lung infection in CF.

[10] Dasenbrook EC, Merlo CA, Diener-West M, et al. "Persistent Methicillin-resistant Staphylococcus aureus and Rate of FEV1 Decline in Cystic Fibrosis." Am J Respir Crit Care Med 2008;178, 814-821.

[11] Dasenbrook EC, Checkley W, Merlo CA, et al. "Association Between Respiratory Tract Methicillin-Resistant Staphylococcus aureus and Survival in Cystic Fibrosis." JAMA 2010;303, 2386-2392.

[12] Zobell JT, Epps KL, Young DC, Montague M, Olson J, Ampofo K, Chin MJ, Marshall BC, Dasenbrook E. "Utilization of antibiotics for methicillin-resistant Staphylococcus aureus infection in cystic fibrosis." Pediatric Pulmonology (June 2015) Volume 50, Issue 6, pages 552–559.

We believe that inhaled antibiotics, as well as other palliative treatments, will continue to have a central role in the management of CF. Various disease modifying drugs, such as CF Transmembrane Conductance Regulator ("CFTR") modulators, that attempt to address the underlying cause of CF, (i.e. restore or improve the function of the CFTR protein that is defective or dysfunctional in individuals living with CF) have recently been launched. Such disease-modifying drugs, on average, result in modest improvement in lung function and, potentially, slow the rate of lung function decline. Patients on these drugs continue to have chronic infections that require antibiotic treatment, and their lung function continues to decline.

AeroVanc Product Description

AeroVanc is a novel inhaled formulation of vancomycin being developed for the treatment of persistent MRSA lung infection in individuals with CF. Vancomycin is a glycopeptide antibiotic that was discovered in the mid-1950's and is commonly used in the prophylaxis and treatment of infections caused by Gram-positive bacteria. Vancomycin acts by inhibiting proper cell wall synthesis of aerobic and anaerobic Gram-positive bacteria, and is generally not active against Gram-negative bacteria.

AeroVanc is delivered via a capsule containing a proprietary dry powder formulation of vancomycin hydrochloride intended for oral inhalation with the AeroVanc inhaler. The AeroVanc inhaler is a commercialized, hand-held, manually operated, breath-activated device manufactured by Plastiape S.p.A. (Lecco, Italy).

We anticipate that AeroVanc will be used predominantly to suppress chronic MRSA lung infection, which has the potential to improve patients' lung function and respiratory symptoms, and to prolong the time to pulmonary exacerbation and need of systemic antibiotics. AeroVanc is not intended to replace IV vancomycin or other IV antibiotics in the treatment of acute pulmonary exacerbations associated with MRSA. However, long-term AeroVanc use has the potential to reduce the occurrence of these exacerbations, and thereby reduce the need for IV treatments and hospitalizations.

If approved, we believe AeroVanc in CF will be broadly adopted based on a high level of interest for the product from direct clinician surveys, as well as market research of key opinion leaders in the field of CF. Notably, a clear majority of the surveyed CF physicians in the U.S. (94%) indicated they expect to prescribe AeroVanc for MRSA lung infection, if approved by the FDA. Likewise, according to U.S. payer interviews, an AeroVanc launch would receive reimbursement support given the high unmet need in an orphan indication and a current lack of comparable products.

AeroVanc Key Advantages

There are a number of important characteristics that, we believe, contribute to AeroVanc's overall clinical profile and may facilitate regulatory approval and, potentially, successful commercialization. Specifically, AeroVanc offers:

- Strong product foundation, applying both a previously approved active drug substance and drug delivery technology.

- High concentration of antibiotic delivered directly to the lungs (the primary site of infection) which, we believe, can result in higher clinical efficacy and reduced systemic toxicity, as compared with oral or IV delivery of antibiotics.

- Capsule based powder inhaler providing a fast and convenient method of administration, which is attractive to the CF population, who have a high treatment burden.

- Eligibility for strong market protection via orphan drug status, QIDP status, a formulation patent, and an exclusive device supply agreement.

Clinical Development of AeroVanc

Phase 3

AeroVanc is currently being investigated in a pivotal Phase 3 clinical study in the U.S. and Canada, called AVAIL, for the treatment of persistent MRSA lung infection in people living with CF. The study began enrolling patients at U.S. and Canadian clinical sites in September 2017 and December 2017, respectively.

AVAIL is currently enrolling approximately 200 patients (150 patients ≤ 21 years old, 50 patients > 21 years old). During Period 1 of the study, patients are randomly assigned in a blinded 1:1 fashion to receive either AeroVanc (30 mg) twice daily, or placebo, by inhalation for 24 weeks or 3 dosing cycles. A dosing cycle is defined as 28 days of treatment followed by 28 days of observation. During Period 2 of the study, patients receive open-label AeroVanc (30 mg) twice daily for an additional 24 weeks or 3 dosing cycles, to evaluate the long-term safety of AeroVanc.

The primary endpoint is the mean absolute change in FEV1 percent predicted from baseline, which will be analyzed sequentially at week 4 (the end of Cycle 1), week 12 (the end of Cycle 2), and at week 20 (the end of Cycle 3). Analysis of the primary endpoint will be based on patients 6 21 years of age. Secondary endpoints include: (i) time-to-use of another antibiotic medication (oral, IV, and/or inhaled) for pulmonary infection, (ii) the number of successful FEV1-response cycles a patient achieves over Period 1 (weeks 4, 12, and 20), (iii) relative change from baseline in FEV1 percent predicted at weeks 4, 12, and 20, (iv) change from baseline Cystic Fibrosis Questionnaire-Revised scores at weeks 4, 12, and 20 and (v) change from baseline in Cystic Fibrosis Respiratory Symptom Diary-Chronic Respiratory Symptom Score scores at weeks 4, 12, and 20.

We anticipate that AVAIL patient enrollment will be completed in Q3 2019 with top line results expected in Q2 2020.

Completed Clinical Studies

Phase 1 Study

In a Phase 1 single escalating dose study, AeroVanc was shown to be generally well tolerated and safe, with a favorable pharmacokinetic profile. In the study, AeroVanc inhalation powder was administered to 18 healthy volunteers (doses of 16 mg, 32 mg, and 80 mg), and seven patients with CF (doses of 32 mg and 80 mg). AeroVanc demonstrated a relatively slow pulmonary absorption phase (Tmax of 1.33 h - 2.08 h), followed by distribution and elimination comparable to IV administration. The mean absolute bioavailability across all AeroVanc doses was 49% (standard deviation 8%), with no apparent differences observed between the doses. The absolute bioavailability closely corresponds with the pulmonary absorption of vancomycin, considering that vancomycin is not absorbed from the gastrointestinal tract. The mean Cmax of AeroVanc after an 80 mg dose was 618 ng/mL, corresponding to approximately one fifth of the dose adjusted Cmax after a 250 mg dose of IV vancomycin. The dose linearity of AeroVanc, in terms of Cmax and AUC values, was excellent ($R^2 > 0.99$). In the CF patients, all subjects had sputum vancomycin concentrations in high excess of the minimum inhibitory concentration (“MIC”) of vancomycin for MRSA (2 µg/mL) at one hour after the administration of AeroVanc with both the 32 mg and the 80 mg dose (mean of 106 µg/mL and 261 µg/mL, respectively). At later time points, the concentrations decreased, but on average remained above the MIC values for up to 24 hours. Variability in sputum concentrations was high, as expected.

All adverse events in the healthy volunteers were classified as mild, and all events that were considered probably drug-related involved local irritation effects and resolved spontaneously and rapidly (between 15 and 60 minutes). Small reduction in the post-dose FEV1 (7% 11%) was observed in three subjects after the 80 mg dose. None of the subjects required bronchodilator treatment, and the changes were considered by the independent Drug Safety Monitoring Board to be clinically non-significant. In CF patients, chest congestion and/or chest tightness were reported by four of the seven patients, and there appeared to be a slight trend towards more adverse events at the higher dose (80 mg). All reported respiratory adverse events were mild, none of the patients felt distressed, and the events either did not require treatment or resolved after airway clearance and/or albuterol inhalation. Based on the sputum concentration data, dose levels of 32 mg and 64 mg twice a day were selected for use in the Phase 2 study.

Phase 2 Study

In a Phase 2 clinical study in CF patients with persistent MRSA lung infection, AeroVanc met a primary endpoint to reduce MRSA density in sputum, and showed encouraging trends of improvement in lung function, prolongation of the time to use of other antibiotics, and improvement in respiratory symptoms, with best responses in patients below 21 years of age. The consistency of the responses across the different endpoints, as well as the magnitude of change in the younger patients, supported the advancement of the AeroVanc drug candidate into a Phase 3 clinical study. The results of the Phase 2 study were summarized and presented to the FDA in an End of Phase 2 Meeting, and the agency subsequently provided detailed guidance on the design and analysis of our current Phase 3 study, which is described above under the heading “Phase 3.” The key findings of the Phase 2 study are described below.

The Phase 2 study evaluated the safety and efficacy of AeroVanc in CF patients with persistently positive MRSA lung infection. The 28-day, randomized, double-blind, placebo-controlled study enrolled 87 patients. AeroVanc was administered at dose level of 32 mg twice daily (“BID”) or 64 mg BID, with an eight-week follow-up. The study was conducted at 40 sites in the U.S. Quantitative MRSA cultures from spontaneously expectorated sputum samples were used as the primary endpoint of the study. The average baseline values in both active drug cohorts, as well as the placebo cohorts were high, ranging from 6.78 7.65 log 10 colony-forming units (“CFU”) /mL. In the primary endpoint analyses (modified intent-to-treat population), a reduction from baseline in MRSA CFU was observed in the 32 mg and 64 mg dose cohorts pooled, compared to placebo by -0.52 log 10 CFU/mL and -0.06 log 10 CFU/mL for the AeroVanc and placebo doses, respectively ($p = 0.0312$); in the 64 mg dose cohort by -0.63 log 10 CFU/mL and 0.16 log 10 CFU/mL for the AeroVanc and placebo doses, respectively ($p = 0.0145$); in the 32 mg dose cohort by -0.25 log 10 CFU/mL and -0.30 log 10 CFU/mL for the AeroVanc and placebo doses, respectively ($p = 0.8352$).

MICs of vancomycin for MRSA cultured from the sputum samples were determined using a broth microdilution technique at baseline, at each visit during the administration of AeroVanc, as well as at the post-administration follow-up time points. The distribution of MIC values was very narrow, with the MIC 50 and MIC 90 both at 0.5 µg/mL at baseline. At baseline, all strains were susceptible to vancomycin, with MIC values of 1 µg/mL, and there were no notable changes in the MIC distribution at any of the time points following the baseline sample. This suggests the susceptibility of MRSA to vancomycin was not affected by the 28 days of pulmonary administration of AeroVanc.

Vancomycin peak and trough concentrations in sputum at Day 8 and Day 29 were in high excess over the generally accepted level of MIC (mean C trough /MIC ratio > 35) after multiple dosing in all patients at both dose levels, with apparent dose-dependency, but no notable difference in C trough between the two time points.

The most frequent adverse events reported were respiratory related. The AeroVanc 32 mg BID dose was well tolerated, with no significant difference in adverse events as compared with placebo. However, a higher incidence of adverse events, most frequently consistent with signs and symptoms of bronchoconstriction, and a significantly higher rate of premature study drug discontinuations were seen in adult patients at the 64 mg BID dose, as compared with patients receiving the 32 mg of AeroVanc or placebo. Discontinuations were most commonly due to drug intolerability (mainly bronchoconstriction and/or chest tightness) or pulmonary exacerbation, and typically occurred within the first two weeks from the start of drug administration.

Based on the observed clinical results in the 32 mg cohort of patients below 21 years of age, the high vancomycin concentrations in sputum observed at both dose levels, and the high frequency of discontinuation in adult patients at the 64 mg dose, the Phase 3 study is further evaluating the 32 mg dose, and enrollment is focused on patients below 21 years of age.

Human Factor Study

We have performed a human factor study with fourteen people living with CF (ages 12 56 years old) to better understand patient reactions to the AeroVanc inhaler device, drug capsule and written instructions. Study participants represented a variety of sex and ethnicity demographics, as well as dominant hand preference. Patients were given the device, capsules and instructions to simulate use (without drug) and provide feedback. In summary, all patients were able to use the device properly and no device design issues were identified that could impact proper use.

Manufacturing and Supply

We do not own or operate manufacturing facilities to produce clinical or commercial quantities of any of our product candidates. We have fee-for-service contracts with well-established drug substance manufacturers, as well as drug product manufacturers covering all steps of the manufacturing process of our product candidates. We expect to

continue with this outsourcing model for the foreseeable future. All of our manufacturing and supply vendors conduct their operations under current Good Manufacturing Practices (“cGMP”), a regulatory standard for the manufacture of pharmaceuticals.

Molgradex Manufacturing

The drug substance in Molgradex, molgramostim, is currently manufactured by GEMA Biotech S.A. (Buenos Aires, Argentina). All clinical and nonclinical studies to date have used material sourced from GEMA Biotech S.A. and validation activities are ongoing to prepare for commercial manufacturing.

The drug product, Molgradex, has been manufactured at Miltenyi Biotec GmbH (Berglisch Gladbach, Germany). Patheon UK Limited (Ferentino, Italy), a division of Thermo Fisher Scientific Inc., has been selected as the commercial drug product manufacturer. Technology transfer is ongoing, and the planning of process validation activities has been initiated.

Molgradex is administered to the lungs using the investigational eFlow® Nebulizer System, manufactured by PARI Pharma GmbH (Stamberg, Germany). The eFlow nebulizer has been CE certified (CE 0123) according to the Medical Devices Directive 93/42/EEC (as amended by Directive 2007/47/EC) as a class IIa device. The device has a 510(k) approval in the U.S. as a general device. We have an exclusive license and a long-term supply agreement with PARI Pharma GmbH, as further discussed below, covering the eFlow nebulizer for the administration of recombinant human GM-CSF.

AeroVanc Manufacturing

AeroVanc is a high-performance inhalation powder formulation of vancomycin hydrochloride, applying a commercially-available capsule inhaler. The drug substance used in AeroVanc, vancomycin hydrochloride USP, is produced using microbial fermentation followed by purification, and is sourced from Xellia Pharmaceuticals ApS (Copenhagen, Denmark), a commercial manufacturer with two manufacturing facilities (one in China and one in Denmark). Both sites use the same cell line and manufacturing processes and produce material of comparable quality. A long-term commercial supply agreement has been established with Xellia Pharmaceuticals ApS.

AeroVanc inhalation powder is a spray-dried powder containing a ratio of 9:1 by weight of vancomycin hydrochloride and l-leucine. L-leucine is an essential amino acid and has generally regarded as safe, GRAS, status as a food additive. Formulation studies showed that the addition of l-leucine improves inhalation performance in vitro, as measured by improved emitted dose and fine particle dose. The powder manufacturing is carried out by Hovione LLC (East Windsor, NJ), a vendor with two operational sites (one in the U.S. and one in Europe). Both of the facilities have the same base equipment, which could be upgraded to produce material of comparable quality. The proprietary AeroVanc spray drying process creates very fine particles (smaller than five microns) required for efficient delivery to the lungs. Proprietary nozzle and cyclone technologies were developed to meet product performance and manufacturing throughput requirements. The powder production process has been successfully scaled-up from laboratory to commercial equipment. A long-term commercial supply agreement is under negotiation with Hovione LLC.

The drug product is manufactured from bulk AeroVanc powder by GlaxoSmithKline Trading Services Limited (“GSK”). At this final stage of manufacturing, AeroVanc powder is conditioned and automatically filled into 16 mg capsules of vancomycin. The capsules are then packaged into aluminum foil blisters to protect them from light and moisture. A long-term commercial supply agreement has been established with GSK for the finished product.

The inhaler device used for AeroVanc is manufactured by Plastiape S.p.A. (Lecco, Italy). The device was approved in the U.S. as part of the Aridol ® new drug application (NDA 022368) on October 5, 2010. A cosmetically modified version of the device was approved in the U.S. as part of the Arcapta ® Neohaler ® new drug application (NDA 022383) on July 1, 2011. An exclusive long-term commercial supply agreement has been established with Plastiape S.p.A.

We have worked with our manufacturing partners to scale up processes, improve yields and production rates, and transfer processes to commercial facilities with commercial equipment. We have produced the supplies for the AVAIL pivotal Phase 3 clinical study using the same manufacturing sites, equipment and processes that will be used for commercial supply.

Commercialization

We own exclusive rights to Molgradex and AeroVanc in the U.S., and all other major markets, except for Japan, where we have licensed the Molgradex rights to Nobelpharma Co., Ltd. (“Nobelpharma”), located in Tokyo, Japan, and which is described further below. We plan to pursue regulatory approvals for our products in the U.S. and EU, and to

independently commercialize AeroVanc and Molgradex in the U.S. In doing so, we may engage with strategic partners to help implement optimal sales and promotion activities. Our commercialization strategy will target key prescribing physicians, as well as provide patients with support programs to ensure product access. Pending EMA approval, we expect to commercialize Molgradex and AeroVanc in certain key markets in the EU and may engage with strategic partners to optimize sales and promotion activities in the remaining EU territories.

License and Supply Agreements

Plastiape S.p.A.

In September 2012, we entered into a supply agreement related to AeroVanc with Plastiape S.p.A, which was subsequently amended in June 2016 (the “Plastiape Agreement”). Pursuant to the terms of the Plastiape Agreement, Plastiape S.p.A. will supply dry powder inhalers to us on an exclusive basis for use with vancomycin for the diagnosis, management, prevention or treatment of lung diseases. Pricing under the Plastiape Agreement is on a per unit basis, with the per unit price decreasing as the volume increases.

Xellia Pharmaceuticals ApS

In September 2016, we entered into a supply agreement related to the supply of the Active Pharmaceutical Ingredients (“API”) for AeroVanc with Xellia Pharmaceuticals ApS (the “Xellia Agreement”). Pursuant to the Xellia Agreement, we are obligated to purchase all of our requirements of the API from Xellia Pharmaceuticals ApS. The pricing under the Xellia Agreement is a set price per kg, with the price decreasing upon the commercial launch of AeroVanc.

PARI Pharma GmbH

In November 2014, Serendex, predecessor-in-interest to our Savara ApS subsidiary, entered into a license and collaboration agreement related to Molgradex with PARI Pharma GmbH ("PARI"), (collectively the "PARI License Agreement"), which we assumed as part of the Serendex Acquisition (refer to Item 7 of this report). Under the PARI License Agreement, we have a worldwide, exclusive license to commercialize PARI's investigational eFlow Nebulizer device for the pulmonary delivery of any liquid formulation containing Human Granulocyte Macrophage Colony Stimulating Factors ("hGM-CSF") as the sole active pharmaceutical ingredient for nebulization for aPAP. Additionally, we have the option to change the device, subject to certain conditions, to PARI's eFlow Technology Nebulizer CS and, until marketing approval, the option to negotiate an extension to the license to cover commercialization of the drug for pulmonary delivery via the PARI eFlow Inline device for the treatment of certain other indications.

On July 23, 2018, we entered into Amendment No. 1 (the "PARI Amendment"), effective May 23, 2018, to the PARI License Agreement which adds NTM lung infection to the indications included in the license and allows us to add other pulmonary infections to the included indications in the future.

Under the terms of the PARI License Agreement, we are not permitted to work with third parties to develop any inhalation device or nebulizer for the pulmonary delivery of a pharmaceutical product containing hGM-CSF as the sole active ingredient. This restriction extends until (i) in the European Economic Area, marketing approval of the product in Europe or the U.S., whichever is later, or (ii) in the rest of the world, the term of the PARI License Agreement.

In consideration of rights granted by PARI, Serendex paid a one-time upfront fee and agreed to pay an hourly rate for work performed by PARI under work orders issued pursuant to the PARI License Agreement. Additionally, we are obligated to make future milestone payments to PARI based upon (i) the successful completion of certain clinical trials, (ii) submissions for regulatory approval in the U.S, the European Union or Japan, and (iii) the first marketing approval for the product in the U.S., the European Union or Japan. The PARI Amendment expanded the development milestones in the agreement to include NTM and any additional pulmonary indications.

If we successfully commercialize any product candidate subject to the PARI License Agreement in a country, we are responsible for royalty payments equal to a percentage of net sales. We are obligated to make such royalty payments until the later of (i) the expiration of the last valid claim in an issued patent covering a portion of the PARI device in the applicable country or (ii) 15 years after the first commercial sale of Molgradex with the PARI device in that country (the "PARI Royalty Period"). If there is no such valid patent claim covering the applicable PARI device, the royalty owed to PARI will be decreased by a specified percentage.

The license term extends on a country by country basis until the end of the PARI Royalty Period or until mutually agreed by the parties.

In April 2015, Serendex entered into a commercial supply agreement with PARI (the "PARI Supply Agreement") related to the supply of the investigational PARI eFlow Technology Nebulizer and related accessories for commercial use with our products after marketing approval is obtained. We assumed the PARI Supply Agreement as part of the Serendex Acquisition (as described in the subheading "Acquisition of Serendex Pharmaceuticals" in Item 7 of this report). Pursuant to the terms of the PARI Supply Agreement, we are obligated to purchase from PARI (i) within the European Economic Area, (a) during the first five years from marketing approval, all of our requirements for the device and related accessories and (b) thereafter 80% and (ii) in the rest of the world, all of our requirements during the PARI Royalty Period. Pricing is on a per unit basis, with a reduction in price once purchasing volumes reach over 5,000 for devices and starter kits and over 40,000 for nebulizer handsets in a twelve-month period.

GEMA Biotech S.A.

In December 2012, Serendex entered into a supply and license agreement related to supplying the API for Molgradex with GEMA Biotech S.A. ("GEMA"), which was subsequently amended by addendums in February 2016 and September 2017 (the "GEMA Agreement"). We assumed the GEMA Agreement as part of the Serendex Acquisition (as described in the subheading "Acquisition of Serendex Pharmaceuticals" in Item 7 of this report). Under the GEMA Agreement, we have an exclusive license to market, distribute and sell products based on GEMA recombinant hGM-CSF for any disease to be treated by inhalation, local pulmonary administration, parenteral administration, or local administration of the API in any territory except Latin America, Central America and Mexico. Under the original GEMA Agreement, GEMA is the sole supplier of the API.

As consideration for the rights granted by GEMA, we are required to pay GEMA an agreed upon price per vial of 1 gram of the API. Additionally, if we successfully develop, register and obtain approval by the proper health authorities, we must pay GEMA a single digit percentage royalty on annual net sales. There is no minimum royalty, and no signing fee or milestones are included in the royalty payments. Additionally, we have milestone-based commitments to GEMA in the amount of $600,000 upon the successful release of the first GMP grade API batch and $2,000,000 upon the first regulatory approval of Molgradex in Europe or the U.S.

Pursuant to the terms of the February 2016 addendum, GEMA granted an exclusive worldwide license to Serendex to transfer the manufacture of the API to Synco Bio Partners B.V., and agreed to transfer the master cell bank and working cell bank to Serendex (now us) at our discretion. Upon the completion of the transfer of the master cell bank and working cell bank, the royalty payable to GEMA described above decreases.

Nobelpharma Co., Ltd.

Serendex entered into a license agreement on May 12, 2016, as assumed by us in the Serendex Acquisition, which was amended on June 4, 2018 (the "Nobelpharma Agreement"), with Nobelpharma Co. Ltd. ("Nobelpharma") under which Nobelpharma received an exclusive right to import, market, sell, distribute and promote Molgradex in Japan for the treatment of aPAP. In return, Nobelpharma will pay us marketing and regulatory-based milestone payments totaling $10.5 million and sales-based royalties equal to thirty-five percent (35%) of the National Health Insurance price determined by the Ministry of Health Labor and Welfare in Japan.

Pursuant to the Nobelpharma Agreement, we are obligated to fund Nobelpharma fifty percent (50%), up to a maximum of approximately $0.8 million, of the external costs associated with specific regulatory and filing activities to be conducted by Nobelpharma regarding the commercialization of Molgradex for the treatment of aPAP in Japan.

Mayo Foundation for Medical Education Services and Research

Under an agreement with the Mayo Foundation for Medical Education Services and Research, entered into on October 8, 2018, we are subject to certain milestone payments for the use of proprietary information and material in specific intellectual property filings related to the application of Molgradex in the treatment of NTM. We will owe royalties to the foundation based on net sales of Molgradex for the treatment of NTM equal to one half of one percent (0.5%) when the intellectual property filings are published and one quarter of one percent (0.25%) prior to the publication or in the event publication does not occur, with respect to the specified intellectual property filings.

Government Regulation

The FDA and other regulatory authorities at federal, state, and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring, and post-approval reporting of drugs, such as those we are developing. We, along with third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of our product candidates. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations require the expenditure of substantial time and financial resources.

Government Regulation of Drugs

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

- Completion of preclinical laboratory tests and animal studies performed in accordance with the FDA's current Good Laboratory Practices ("GLP") regulation.
- Submission to the FDA of an IND, which must become effective before clinical trials may begin and must be updated annually or when significant changes are made.
- Approval by an independent Institutional Review Board ("IRB") or ethics committee for each clinical site before a clinical trial can begin.
- Performance of adequate and well-controlled human clinical trials to establish the safety, purity and potency of the proposed product candidate for its intended purpose.
- Preparation of and submission to the FDA of an NDA, after completion of all required clinical trials.
- A determination by the FDA within 60 days of its receipt of an NDA to file the application for review.
- Satisfactory completion of an FDA Advisory Committee review, if applicable.

- Satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with cGMPs and to assure that the facilities, methods and controls are adequate to preserve the product's continued safety, purity and potency, and of selected clinical investigational sites to assess compliance with current Good Clinical Practices ("cGCP"); and
- FDA review and approval of the NDA to permit commercial marketing of the product for particular indications for use in the U.S., which must be updated annually and when significant changes are made.

The testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all. Prior to beginning the first clinical trial with a product candidate, we must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and in vitro studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with cGCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. Furthermore, an independent IRB, for each site proposing to conduct the clinical trial, must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site, and must monitor the study until completed. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

For purposes of NDA approval, human clinical trials are typically conducted in three sequential phases that may overlap. Additionally, in certain instances, a fourth phase, post approval, may be necessary or required.

- Phase 1. The drug product is initially introduced into healthy human subjects and tested for safety. In the case of some products for severe or life-threatening diseases, the initial human testing is often conducted in patients.
- Phase 2. The drug product is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.
- Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy, potency, and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk to benefit ratio of the product and provide an adequate basis for product labeling.
- Phase 4. In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. Phase 4 studies may be required as a condition to approval of the NDA.

Phase 1, Phase 2 and Phase 3 testing may not be completed successfully within a specified period, if at all, and there can be no assurance that the data collected will support FDA approval or licensure of the product. Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the drug characteristics of the product candidate, and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

NDA Submission and Review by the FDA

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, nonclinical studies and clinical trials are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. The NDA must include all relevant data available from pertinent preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of a use of the product, or from a number of alternative sources, including studies initiated by investigators. The submission of an NDA requires payment of a substantial user fee to the FDA, and the sponsor of an approved NDA is also subject to annual product and establishment user fees. These fees are typically increased annually. A waiver of user fees may be obtained under certain limited circumstances.

Within 60 days following submission of the application, the FDA reviews an NDA to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any NDA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the NDA must be resubmitted with the additional information. Once an NDA has been filed, the FDA's goal is to review the application within ten months after it accepts the application for filing, or, if the application relates to an unmet medical need in a serious or life-threatening indication, six months after the FDA accepts the application for filing. The review process is often significantly extended by FDA requests for additional information or clarification. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for the indication being pursued, and the facility in which it is manufactured, processed, packed, or held meets standards designed to assure the product's continued safety and effectiveness. The FDA may convene an advisory committee to provide clinical insight on application review questions. Before approving an NDA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with cGCP. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

The testing and approval process requires substantial time, effort and financial resources, and each may take several years to complete. The FDA may not grant approval on a timely basis, or at all, and we may encounter difficulties or unanticipated costs in our efforts to secure necessary governmental approvals, which could delay or preclude us from marketing our products. After the FDA evaluates an NDA and conducts inspections of manufacturing facilities where the investigational product and/or our drug substance will be produced, the FDA may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter may request additional information or clarification. The FDA may delay or refuse approval of an NDA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If regulatory approval of a product is granted, such approval may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the NDA with a Risk Evaluation and Mitigation Strategy ("REMS") to mitigate risks, 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 or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing regulatory standards is not maintained or if problems occur after the product reaches the

marketplace. The FDA may require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies. In addition, 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 its products under development.

A sponsor may seek approval of its product candidate under programs designed to accelerate the FDA's review and approval of new drugs that meet certain criteria. Specifically, new drug products 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. For a fast track product, the FDA may consider sections of the NDA for review on a rolling basis before the complete application is submitted if relevant criteria are met. A fast track designated product candidate may also qualify for priority review, under which the FDA sets the target date for FDA action on the NDA at six months after the FDA accepts the application for filing. Priority review is granted when there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious condition. If criteria are not met for priority review, the application is subject to the standard FDA review period of 10 months after FDA accepts the application for filing. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Under the accelerated approval program, the FDA may approve an NDA on the basis of either a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Post-marketing studies or completion of ongoing studies after marketing approval are generally required to verify the biologic's clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit. In addition, the U.S. Food and Drug Administration Safety and Innovation Act, which was enacted and signed into law in 2012, established breakthrough therapy designation. A sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the product candidate is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Sponsors may request the FDA to designate a breakthrough therapy at the time of or any time after the submission of an IND, but ideally before an end-of-phase 2 meeting with the FDA. If the FDA designates a breakthrough therapy, it may take actions appropriate to expedite the development and review of the application, which may include holding meetings with the sponsor and the review team throughout the development of the therapy; providing timely advice to, and interactive communication with, the sponsor regarding the development of the drug to ensure that the development program to gather the nonclinical and clinical data necessary for approval is as efficient as practicable; involving senior managers and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review; assigning a cross-disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor; and considering alternative clinical trial designs when scientifically appropriate, which may result in smaller or more efficient clinical trials that require less time to complete and may minimize the number of patients exposed to a potentially less efficacious treatment. Breakthrough designation also allows the sponsor to file sections of the NDA for review on a rolling basis. We may seek designation as a breakthrough therapy for some or all of our product candidates.

Fast track designation, priority review and breakthrough therapy designation do not change the standards for approval but may expedite the development or approval process.

The review and approval process with respect to our drug candidates may also be significantly delayed in the event of government shutdowns, if any.

Orphan Drug Status

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drug candidates intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the U.S., or more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that costs of research and development of the drug for the indication can be recovered by sales of the drug in the U.S. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Although there may be some increased communication opportunities, orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a drug candidate that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including a full NDA, to market the same drug for the same indication for seven years, except in very limited circumstances, such as if the second applicant demonstrates the clinical superiority of its product or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug for

the same disease or condition, or the same drug for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee.

Orphan drug exclusivity could block the approval of our drug candidates for seven years if a competitor obtains approval of the same product as defined by the FDA or if our drug candidate is determined to be contained within the competitor's product for the same indication or disease.

As in the U.S., designation as an orphan drug for the treatment of a specific indication in the EU, must be made before the application for marketing authorization is made. Orphan drugs in Europe enjoy economic and marketing benefits, including up to 10 years of market exclusivity for the approved indication unless another applicant can show that its product is safer, more effective or otherwise clinically superior to the orphan designated product.

The FDA and foreign regulators expect holders of exclusivity for orphan drugs to assure the availability of sufficient quantities of their orphan drugs to meet the needs of patients. Failure to do so could result in the withdrawal of marketing exclusivity for the orphan drug.

GAIN Act Exclusivity for Antibiotics

In 2012, Congress passed legislation known as the Generating Antibiotic Incentives Now Act (the "GAIN Act"). This legislation is designed to encourage the development of antibacterial and antifungal drug products that treat pathogens that cause serious and life-threatening infections. To that end, the new law grants an additional five years of exclusivity upon the approval of an NDA for a drug product designated by FDA as a QIDP. Thus, for a QIDP with Orphan Drug Designation, the periods of five-year exclusivity and seven-year orphan drug exclusivity, would become 12 years.

A QIDP is defined in the GAIN Act to mean "an antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections, including those caused by (1) an antibacterial or antifungal resistant pathogen, including novel or emerging infectious pathogens or (2) certain qualifying pathogens." A "qualifying pathogen" is a pathogen that has the potential to pose a serious threat to public health (such as resistant Gram-positive pathogens, multi-drug resistant Gram-negative bacteria, multi-drug resistant tuberculosis, and C. difficile) and that is included in a list established and maintained by the FDA. A drug sponsor may request the FDA to designate its product as a QIDP any time before the submission of an NDA. The FDA must make a QIDP determination within 60 days of the designation request. A product designated as a QIDP will be granted priority review by the FDA and can qualify for "fast track" status.

The five year exclusivity extension under the GAIN Act for drug products designated by the FDA as QIDPs does not apply to: a supplement to an application under FDCA Section 505(b) for any QIDP for which an extension is in effect or has expired; a subsequent application filed with respect to a product approved by the FDA for a change that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength; or a product that does not meet the definition of a QIDP under Section 505(g) based upon its approved uses.

Post-Approval Requirements

Any products manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record keeping, reporting of adverse experiences, periodic reporting, distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance. We cannot be certain that we or our present or future suppliers will be able to comply with the cGMP regulations and other FDA regulatory requirements. If our present or future suppliers are not able to comply with these requirements, the FDA may, among other things, halt our clinical trials, require us to recall a product from distribution, or withdraw approval of the NDA.

Future FDA and state inspections may identify compliance issues at our facilities or at the facilities of our contract manufacturers 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.

The FDA may withdraw approval of an NDA if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;

- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of drugs and biologics. A company can make only those claims relating to safety and efficacy that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

Government Regulation of Combination Products

Our products under development will be regulated as combination products, which means that they are comprised of two or more different components that, if marketed individually, would be subject to different regulatory paths and would require approval of independent marketing applications by the FDA. A combination product, however, is assigned to a center within the FDA that will have primary jurisdiction over its regulation on a determination of the combination product's primary mode of action, which is the single mode of action that provides the most important therapeutic action. We believe our product candidates include both a drug and medical device component, and will be regulated as a drug, subject to the review of the FDA's Center for Drug Evaluation and Research which will have primary jurisdiction over premarket development and approval. The FDA's Center for Devices and Radiological Health will provide support and review of the inhaler component of our product candidates.

Other Healthcare Laws and Compliance Requirements

Our sales, promotion, medical education, clinical research and other activities following product approval will be subject to regulation by numerous regulatory and law enforcement authorities in the U.S. in addition to the FDA, including potentially the Federal Trade Commission, the Department of Justice, the Centers for Medicare and Medicaid Services, other divisions of the U.S. Department of Health and Human Services and state and local governments. Our promotional and scientific/educational programs and interactions with healthcare professionals must comply with the federal Anti-Kickback Statute, the civil False Claims Act ("FCA"), physician payment transparency laws, privacy laws, security laws, and additional federal and state laws similar to the foregoing.

The federal Anti-Kickback Statute prohibits, among other things, the knowing and willing, direct or indirect offer, receipt, solicitation or payment of remuneration in exchange for or to induce the referral of patients, including the purchase, order or lease of any good, facility, item or service that would be paid for in whole or part by Medicare, Medicaid or other federal health care programs. Remuneration has been broadly defined to include anything of value, including cash, improper discounts, and free or reduced-price items and services. The federal Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, formulary managers, and beneficiaries on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to increased scrutiny and review if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the federal Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all its facts and circumstances. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the federal Anti-Kickback Statute

has been violated. The government has enforced the federal Anti-Kickback Statute to reach large settlements with healthcare companies based on sham research or consulting and other financial arrangements with physicians. Further, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA. Many states have similar laws that apply to their state health care programs as well as private payers.

Federal false claims and false statement laws, including the FCA, impose liability on persons and/or entities that, among other things, knowingly present or cause to be presented claims that are false or fraudulent or not provided as claimed for payment or approval by a federal health care program. The FCA has been used to prosecute persons or entities that "cause" the submission of claims for payment that are inaccurate or fraudulent, by, for example, providing inaccurate billing or coding information to customers, promoting a product off-label, submitting claims for services not provided as claimed, or submitting claims for services that were provided but not medically necessary. Actions under the FCA may be brought by the Attorney General or as a qui tam action by a private individual, or whistleblower, in the name of the government. Violations of the FCA can result in significant monetary penalties and treble damages. The federal government is using the FCA, and the accompanying threat of significant liability, in its investigation and prosecution of pharmaceutical and biotechnology companies throughout the country, for example, in connection with the promotion of products for unapproved uses and other illegal sales and marketing practices. The government has obtained multi-million and multi-billion dollar settlements under the FCA in addition to individual criminal convictions under applicable criminal statutes. In addition, certain companies that were found to be in violation of the FCA have been forced to implement extensive corrective action plans, and have often become subject to consent decrees or corporate integrity agreements, restricting the manner in which they conduct their business.

The federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payers; 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 healthcare benefits, items or services; and willfully obstructing a criminal investigation of a healthcare offense. Like the federal Anti-Kickback Statute, the Affordable Care Act amended the intent standard for certain healthcare fraud statutes under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

Given the significant size of actual and potential settlements, it is expected that the government will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable fraud and abuse laws. Also, many states have similar fraud and abuse statutes or regulations that may be broader in scope and may apply regardless of payer, in addition to items and services reimbursed under Medicaid and other state programs. Additionally, to the extent that our products, once commercialized, are sold in a foreign country, we may be subject to similar foreign laws.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the Affordable Care Act, among other things, imposed new reporting requirements on certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, for payments or other transfers of value made by them to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Covered manufacturers are required to collect and report detailed payment data and submit legal attestation to the accuracy of such data to the government each year. Failure to submit required information may result in civil monetary penalties of up to an aggregate of $150,000 per year (or up to an aggregate of $1 million per year for "knowing failures"), for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Additionally, entities that do not comply with mandatory reporting requirements may be subject to a corporate integrity agreement. Certain states also mandate implementation of commercial compliance programs, impose restrictions on covered manufacturers' marketing practices and/or require the tracking and reporting of gifts, compensation and other remuneration to physicians and other healthcare professionals.

We are also subject to data privacy and security regulation by the federal government and the states in which we conduct our business and the EU with the General Data Protection Regulation rules which became effective in May 2018. HIPAA, as amended by the Health Information Technology and Clinical Health Act ("HITECH"), and their

respective implementing regulations, imposes specified requirements on certain health care providers, plans and clearinghouses (collectively, “covered entities”) and their “business associates,” relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA’s security standards directly applicable to “business associates,” defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney’s fees and costs associated with pursuing federal civil actions. In addition, certain states have their own laws that govern the privacy and security of health information in certain circumstances, many of which differ from each other and/or HIPAA in significant ways and may not have the same effect, thus complicating compliance efforts.

If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to them, we may be subject to penalties, including, without limitation, civil and criminal penalties, damages, fines, disgorgement, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs, imprisonment, contractual damages, reputational harm, and diminished profits and future earnings, any of which could adversely affect our ability to operate our business and our financial results.

In addition to the foregoing health care laws, we are also subject to the U.S. Foreign Corrupt Practices Act ("FCPA") and similar worldwide anti-bribery laws, which generally prohibit companies and their intermediaries from making improper payments to government officials or private-sector recipients for the purpose of obtaining or retaining business. We have adopted an anti-corruption policy which mandates compliance with the FCPA and similar anti-bribery laws applicable to our business throughout the world. However, we cannot assure that such a policy or procedures implemented to enforce such a policy will protect against intentional, reckless or negligent acts committed by our employees, distributors, partners, collaborators or agents. Violations of these laws, or allegations of such violations, could result in fines, penalties or prosecution and have a negative impact on our business, results of operations, and reputation.

Coverage and Reimbursement

Sales of pharmaceutical products depend significantly on the extent to which coverage and adequate reimbursement are provided by third-party payers. Third-party payers include state and federal government health care programs, managed care providers, private health insurers and other organizations. Although we currently believe that third-party payers will provide coverage and reimbursement for our product candidates, if approved, we cannot be certain of this. Third-party payers are increasingly challenging the price, examining the cost-effectiveness, and reducing reimbursement for medical products and services. In addition, significant uncertainty exists as to the reimbursement status of newly approved healthcare products. The U.S. government, state legislatures and foreign governments have continued implementing cost containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Adoption of price controls and cost containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could limit our net revenue and results. We may need to conduct expensive clinical studies to demonstrate the comparative cost-effectiveness of our products. The product candidates that we develop may not be considered cost-effective and thus may not be covered or sufficiently reimbursed. It is time consuming and expensive for third-party payers to seek coverage and reimbursement. Thus, one payer's decision to provide coverage and adequate reimbursement for a product does not assure that another payer will provide coverage or that the reimbursement levels will be adequate. Moreover, a payer's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Reimbursement may not be available or sufficient to allow third-party payers to sell our products on a competitive and profitable basis.

Healthcare Reform

The U.S. and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change the healthcare system in ways that could materially affect our ability to sell our products profitably. Among policy makers and payers in the U.S. and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the U.S., the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

By way of example, in March 2010, the Affordable Care Act was signed into law, intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Among the provisions of the Affordable Care Act of importance to our potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for a manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. These changes include, among others, the Budget Control Act of 2011, which mandates aggregate reductions to Medicare payments to providers of up to 2% per fiscal year effective April 1, 2013, and due to subsequent legislative amendments, will remain in effect through 2024 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our product candidates, if approved, and, accordingly, our financial operations.

We expect that healthcare reform measures that may be adopted in the future, including the possible repeal and replacement of the Affordable Care Act, are unpredictable, and the potential impact on our operations and financial position are uncertain, but may result in more rigorous coverage criteria and lower reimbursement, and place additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our drugs.

Foreign Regulation

In addition to regulations in the U.S., we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products to the extent we choose to develop or sell any products outside of the U.S. The approval process varies from country to country and the time may be longer or shorter than that required to obtain FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

Intellectual Property

We strive to protect the proprietary technology that we believe is important to our business, including our product candidates and our processes. We seek patent protection in the U.S. and internationally for our products, their methods of use and processes of manufacture and any other technology to which we have rights, as appropriate, such as device exclusivity. We also rely on trade secrets that may be important to the development of our business.

We own six issued patents and additional pending patent applications worldwide for a proprietary formulation of AeroVanc. The patents and pending applications are derived from a PCT application (Pub. No. WO2012159103) entitled "Dry Powder Vancomycin Compositions and Associated Methods." In May 2017, the United States Patent and Trademark Office issued United States Patent No. 9,572,774 for "Dry Powder Vancomycin Compositions and Associated Methods" which will provide key intellectual property protection in the U.S. for the AeroVanc program and will expire no earlier than 2032. This affords us important composition of matter protection for our AeroVanc program in the U.S., the largest market for the product, and is a key component of our market protection strategy which also includes Orphan Drug and QIDP protection. We have also received a Notice of Allowance from the Canadian Intellectual Property Office for our Canadian Patent Application No. 2,836,643 entitled "Dry Powder Vancomycin Compositions and Associated Methods." This notice serves as official communication that the examination of the patent application has been successfully completed. Once issued, the patent will provide protection

for AeroVanc in Canada until 2032. We also have corresponding patent applications for AeroVanc in different stages of prosecution in other key markets throughout the world. As of March 12, 2019, patents have issued in the U.S., Canada, Australia, China, Japan, New Zealand, and Singapore.

While we do not have any issued patents or pending applications covering Molgradex or its use in aPAP, we have issued patents ex-US (under prosecution in the U.S.) with an additional international patent application pending for Molgradex for the treatment of NTM lung infection. Molgradex is also a registered trademark in most European countries.

Our success will, in part, depend on the ability to obtain and maintain patent and other proprietary rights in commercially important technology, inventions and know-how related to our business, the validity and enforceability of our patents, the continued confidentiality of our trade secrets as well as our ability to operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position.

We cannot be sure patents will be granted with respect to any of our pending patent applications or with respect to any patent applications we may own or license in the future, nor can we be sure that any of our existing patents or any patents we may own or license in the future will be useful in protecting our technology and products. For this and more comprehensive risks related to our intellectual property, please see “Risk Factors — Risks Related to Our Intellectual Property.”

Trade Secrets

In addition to patents, we rely on trade secrets and know-how to develop and maintain our competitive position. For example, significant aspects of our processes and proprietary technology portfolio are based on unpatented trade secrets and know-how. Trade secrets and know-how can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and commercial partners. These agreements are designed to protect the proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with a third party. While we have confidence in our key individuals, consultants, partner organizations and systems, agreements or security measures may be breached, and there may not be adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our contractors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Competition

The pharmaceutical industry is highly competitive and subject to continuous technological change. Our potential competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical and generic drug companies, academic institutions, government agencies and research institutions. We believe that key competitive factors affecting the commercial success of our product candidates will be efficacy, safety and tolerability profile, reliability, convenience of dosing, price and reimbursement. Many of our potential competitors, either alone or with their collaboration partners have substantially greater financial, technical and human resources than us, and significantly greater experience in the discovery and development of product candidates, manufacturing, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Accordingly, our competitors may be faster and more successful in obtaining FDA approval for therapies and achieving widespread market acceptance. Mergers and acquisitions in the pharmaceutical and biotechnology industry may result in even more resources being concentrated among a smaller number of very capable competitors. We anticipate facing intense and increasing competition as new drugs enter the market and advanced technologies become available. Our competitors’ products may be more effective, or more effectively marketed and sold, than any product candidate we may commercialize and may render our therapies obsolete or non-competitive before we can recover development and commercialization expenses.

We are not aware of any other companies developing an inhaled form of GM-CSF. A glycosylated GM-CSF product, sargramostim (Leukine), is available on the market in the U.S., intended for IV or subcutaneous delivery in patients with neutropenia following cancer chemotherapy. Leukine has not been approved for the treatment of aPAP or any other acute or chronic lung disease but may be administered off-label. The drug substance in Leukine, sargramostim, has been used in a nonclinical research project conducted by NIH/TRND in collaboration with the University of Cincinnati College of Medicine on the potential application of inhaled GM-CSF as a treatment for aPAP. No clinical studies have been conducted to date under this collaboration project. We are aware of a multicenter clinical study of inhaled Leukine, using a standard commercially available nebulizer, which is currently ongoing in Japan, conducted by a consortium of independent clinical investigators. It is not known to us if this study, together with other possibly available related clinical or nonclinical information, may be, or will be, used to support a potential new product approval in Japan. If such a new product would be approved and launched in Japan, we believe it has the potential to present a material competitive threat to the commercial success of Molgradex in Japan. In addition, in November 2018, Partner Therapeutics, Inc., a commercial biotechnology company, was granted Orphan Drug Designation to

Leukine® for the treatment of PAP by the FDA.

We are not aware of any other companies developing inhaled forms of vancomycin. There are several inhaled antibiotics on the market or in development, but we are not aware of any other inhaled antibiotic product that would be specifically developed for the treatment of MRSA infection. Certain inhaled antibiotics in development, including levofloxacin, and ciprofloxacin inhalation formulations, may possess some level of in vitro or in vivo activity against MRSA, even though the compounds are not generally considered MRSA-antibiotics. It is therefore possible that such products, if approved, may present a competitive threat to AeroVanc. A combination product containing fosfomycin and tobramycin for inhalation ("FTI") was developed by Gilead Sciences (Foster City, CA), and shown in a Phase 2 study to possess activity against Gram-negative and Gram-positive bacteria, including MRSA. Gilead Sciences terminated the development of the product, and licensed it to CURx Pharmaceuticals (San Diego, CA) in February 2014. No clinical studies on FTI have been initiated by CURx Pharmaceuticals. If FTI is developed, and approved, for the treatment of MRSA lung infection in CF, we believe it has the potential to present a material competitive threat to the commercial success of AeroVanc.

Many small and large pharmaceutical companies have intravenously or orally administered MRSA-antibiotics on the market, and/or in development. Whereas such antibiotics are important in the treatment of many acute and chronic MRSA-infections, such as skin and soft tissue infections, pneumonia, or endocarditis, we do not believe these products are practical or sufficiently efficacious and/or safe for long-term management of chronic MRSA lung infection in individuals living with CF. Therefore, we do not believe these products and product candidates are a material competitive threat to the commercial success of AeroVanc.

Employees

As of March 13, 2019, we had 33 full-time employees and one part-time employee, as well as several full-time or part-time consultants. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Acquisition of Serendex Pharmaceuticals

On July 15, 2016, we closed on a Business Transaction Agreement (the “Serendex Acquisition”) under which we acquired certain assets, liabilities, employees, and subsidiaries of Serendex Pharmaceuticals A/S (“Serendex”), a public limited company organized under the laws of Denmark, which delisted from the Oslo Axxes on or about May 4, 2016. Serendex’s wholly-owned subsidiaries include Pharmaorigin ApS and Drugrecure ApS which are private limited companies organized under the laws of Denmark. Serendex was a biopharmaceutical development company which, directly and through its subsidiaries, advanced a pipeline and portfolio of novel inhalation therapies and related technologies for the treatment of severe pulmonary conditions. Its primary focus was on the medicinal product Molgradex (an inhalation formulation of recombinant human GM-CSF for the treatment of aPAP). The purchase price consists of 1,965,400 shares of our common stock, taking into consideration the Exchange Ratio of the Merger (refer to Note 1 of the consolidated financial statement in this report), and $21.5 million of contingent cash consideration based upon the achievement of certain milestones.

Merger with Mast Therapeutics and Corporate Information

On April 27, 2017, Savara completed its business combination with Mast Therapeutics, Inc. (“Mast”), a publicly held company, in accordance with the terms of the Agreement and Plan of Merger and Reorganization (the "Merger Agreement"), dated January 6, 2017 (the ‘Merger’). In connection with and immediately prior to the effective time of the Merger, Mast implemented a reverse stock split at a ratio of one new share for every 70 shares of its common stock outstanding. Under the terms of the Merger Agreement, each outstanding share of Savara common stock was then converted into Mast common stock at the Exchange Ratio (refer to Item 7 and note 1 of the consolidated financial statements included in Item 15 of this report). As a result of the Merger, the Mast’s pre-existing equity holders owned approximately 23% of the combined company, and Savara’s pre-existing equity holders owned approximately 77%. In connection with the Merger, Mast changed its name to Savara Inc.

Savara was formed as a corporation in Delaware in 2007. Mast was originally incorporated in Delaware in December 1995. In October 2000, Mast merged its wholly-owned subsidiary, Biokeys Acquisition Corp., with and into Biokeys, Inc. and changed its name to Biokeys Pharmaceuticals, Inc. In May 2003, Mast merged Biokeys, Inc., a wholly-owned subsidiary, with and into the company and changed the company’s name to ADVENTRX Pharmaceuticals, Inc. In March 2013, the company merged Mast Therapeutics, Inc., a wholly-owned subsidiary, with and into the company and changed the company’s name to Mast Therapeutics, Inc. In April 2017, Mast merged its wholly-owned subsidiary, Victoria Merger Corp., with and into Aravas Inc. (formerly, Savara Inc.) and changed the name of the company to Savara Inc.

Our website is located at http://www.savarapharma.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 ("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 ("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. The SEC maintains a website that contains reports, proxy and information statements, and other information regarding our filings at http://www.sec.gov.

Trademarks

"Savara Inc.," the Savara logo, "AeroVanc," and "Molgradex" are unregistered trademarks of Savara Inc. or its subsidiaries in the U.S. and other jurisdictions. Other third-party logos and product/trade names are registered trademarks or trade names of their respective companies. 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.

Item 1A. Risk Factors.

Investment in our common stock 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 Capital Requirements and Financial Condition

We have a limited operating history and have incurred significant losses since inception and expect that we will continue to incur losses for the foreseeable future, which makes it difficult to assess our future viability.

We are a clinical development-stage biopharmaceutical company with a limited operating history upon which to evaluate our business and prospects. We have not been profitable since we commenced operations and may not ever achieve profitability. In addition, we have limited history as an organization and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical industry. Drug development is a highly speculative undertaking and involves a substantial degree of risk. To date, we have not obtained any regulatory approvals for any of our product candidates, commercialized any of our product candidates or generated any product revenue. We have devoted significant resources to research and development and other expenses related to our ongoing clinical trials and operations, in addition to acquiring product candidates.

For the year ended December 31, 2018, we incurred a net loss of $61.5 million, and net cash used in operating activities was $39.3 million. At December 31, 2018, our cash, cash equivalents and short-term investment securities were $110.8 million, and working capital was $106.1 million. At December 31, 2018, we had an accumulated deficit of $129.7 million. We expect to continue to incur substantial operating losses for the next several years as we seek to advance our product candidates through clinical development, global regulatory approvals, and commercialization. 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 will require additional financing to obtain regulatory approval for Molgradex and AeroVanc, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development efforts or other operations.

Since our Aravas subsidiary was formed in 2007, most of our resources have been dedicated to the development and acquisition of our product candidates, Molgradex and AeroVanc. Under our current operating plan, we believe that our existing capital resources will be sufficient to fund our planned operations into 2020. However, we may raise additional capital, including through our “at the market offering” program, to fund new studies, programs or acquisitions, or to address changes in our existing development programs. We cannot estimate with reasonable certainty the actual amounts necessary to successfully complete the development and commercialization of our product candidates and there is no certainty that we will be able to raise the necessary capital on reasonable terms or at all.

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 our product candidates;
- changes in standards of care which could increase the size and complexity of our clinical studies;
- the number of patients who participate, the rate of enrollment, and the ratio of randomized to evaluable patients in each clinical study;
- the ability to locate patients to participate in a study given the limited number of patients available for orphan or ultra-orphan indications;
- 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;
- 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;
- the costs involved in evaluating competing technologies and market developments or the loss in sales in case of such competition; and
- the costs involved in establishing, enforcing or defending patent claims and other proprietary rights.

Additional capital may not be available when we need it, on terms that are acceptable to us or at all. If adequate funds are not available to us on a timely basis, we will be required to delay, limit, reduce or terminate our establishment of sales and marketing, manufacturing or distribution capabilities, development activities or other activities that may be necessary to commercialize our product candidates, conduct preclinical or clinical studies, or other development activities.

If we raise additional capital through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish certain valuable rights to our product candidates, technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable to us. If we raise additional capital through public or private equity offerings, the ownership interest of our stockholders will be diluted, and the terms of any new equity securities may have preferential rights over our common stock. If we raise additional capital through debt financing, it may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt or making capital expenditures, or subject to specified financial ratios, any of which could restrict our ability to develop and commercialize our product candidates or operate as a business.

Our loan agreement contains covenants which may adversely impact our business; the failure to comply with such covenants could cause our outstanding debt to become immediately payable.

On April 28, 2017, we entered into a Loan and Security Agreement, as subsequently amended on December 4, 2018 to increase the committed facility amount, between us and Aravas, as co-borrowers, and Silicon Valley Bank (the "Amended Loan Agreement"). The Amended Loan Agreement includes a number of restrictive covenants, including restrictions on incurring additional debt, making investments, granting liens, disposing of assets, paying dividends and redeeming or repurchasing capital stock, subject to certain exceptions. Collectively, these covenants could constrain our ability to grow our business through acquisitions or engage in other transactions. In addition, the Amended Loan Agreement includes covenants requiring, among other things, that we provide financial statements, comply with all laws, pay all taxes and maintain insurance. If we are not able to comply with these covenants, the loans under the Amended Loan Agreement could become immediately due and payable and would have a material adverse effect on our liquidity, financial condition, operating results, business, and prospects and cause the price of our common stock to decline.

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, 2018, we had goodwill and IPR&D of approximately $38.3 million. These intangible assets are subject to an impairment analysis whenever an event or change in circumstances indicates the carrying amount of such assets 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. We will continue to evaluate our intangible assets for potential impairment in accordance with our accounting policies.

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 our product candidates, 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.

During the year ended December 31, 2018, we recorded $21.7 million of impairment charges and a corresponding decrease to the carrying value of IPR&D related to the Aironite drug candidate assumed in the Merger (as defined and further described in Note 7 of the Consolidated Financial Statements in this report) due to the unfavorable results from a Phase 2 study that demonstrated a failure of Aironite to meet the endpoints of the study and limited effectiveness of the compound in patients. As a result of the IPR&D impairment charges recorded in the first quarter of 2018, we reduced the associated deferred tax liability related to the acquired IPR&D from the Merger by $4.6 million and recorded an income tax benefit.

Risks Related to Our Business Strategy and Operations

We are substantially dependent upon the clinical, regulatory and commercial success of our product candidates, Molgradex and AeroVanc. Clinical drug development involves a lengthy and expensive process with an uncertain outcome, results of earlier studies and trials may not be predictive of future trial results, and our clinical trials may fail to adequately demonstrate to the satisfaction of regulatory authorities the safety and efficacy of our product candidates.

The success of our business is dependent on our ability to advance the clinical development of Molgradex for the treatment of patients with aPAP, including its expansion into NTM lung infection, and AeroVanc for the treatment of persistent MRSA infections in the lungs of CF patients. The Molgradex Phase 3 clinical study designated as IMPALA is ongoing in Europe, Japan, and the U.S. We expect to announce top-line results from the Phase 3 study of Molgradex at the end of the second quarter of 2019. The AeroVanc Phase 3 study, designated as AVAIL, started in the U.S. and Canada in the third quarter of 2017. We expect to announce top-line results from the Phase 3 study of AeroVanc in the second quarter of 2020.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. A failure of one or more of our clinical trials can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. There is a high failure rate for drugs proceeding through clinical trials, and product candidates in later stages of clinical trials may fail to show the required safety and efficacy despite having progressed through preclinical studies and initial clinical trials. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier clinical trials, and we cannot be certain that we will not face similar setbacks. Even if our clinical trials are completed, the results may not be sufficient to obtain regulatory approval for our product candidates.

Given the developmental nature of our product candidates, we are subject to risks associated with initiating, completing and achieving positive outcomes from our current and future clinical trials, including:

- slow implementation, enrollment and completion of the clinical trials;
- inability to enroll enough patients in the clinical trials;
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low patient compliance and adherence to dosing and reporting requirements, for example incomplete reporting of patient reported outcomes in the clinical trials or missed doses;
- lack of safety and efficacy in the clinical trials;
- delays in manufacture of supplies for both drug and device components due to delays in formulation, process development, or manufacturing activities;
- requirements for additional nonclinical or clinical studies based on changes to formulation and/or changes to regulatory requirements; and
- requirements for additional clinical studies based on inconclusive clinical results or changes in market, standard of care, and/or regulatory requirements.

If we successfully complete the necessary clinical trials for our product candidates, our success will be subject to the risks associated with obtaining regulatory approvals, product launch, and commercialization, including:

- FDA rejection of our NDA and BLA submissions for our product candidates;
- regulatory rejection in the EU, Japan, and other markets;
- delays during regulatory review and/or requirements for additional Chemistry, Manufacturing, and Controls ("CMC"), nonclinical, or clinical studies, resulting in increased costs and/or delays in marketing approval and subsequent commercialization of the product candidates in the U.S. and other markets;
- inability to consistently manufacture commercial supplies of drug and delivery devices resulting in slowed market development and lower revenue;
- poor commercial sales due to:
- the ability of our future sales organization or our potential commercialization partners to effectively sell the product candidates;
- our lack of success in educating physicians and patients about the benefits, administration and use of our product candidates;
- the availability, perceived advantages, relative cost, relative safety and relative efficacy of other products or treatments for the targeted indications of the product candidates;
- low patient demand for the product candidates; and
- poor prescription coverage and inadequate reimbursement for our product candidates;
- our inability to enforce our intellectual property rights in our product candidates; and
- reduction in the safety profile of our product candidates following approval.

Many of these clinical, regulatory and commercial matters are beyond our control and are subject to other risks described elsewhere in this "Risk Factors" section. Accordingly, we cannot assure that we will be able to advance our product candidates further through final clinical development, or obtain regulatory approval of, commercialize or generate significant revenue from them. If we cannot do so, or are significantly delayed in doing so, our business will be materially harmed.

If we fail to attract and retain senior management and key scientific personnel, we may be unable to successfully develop and commercialize our product candidates.

We have historically operated with a limited number of employees that manage third-parties for most development activities. Institutional knowledge is concentrated within a small number of employees. Our success depends on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel. Our future success is highly dependent upon the contributions of our senior management, as well as our senior scientists and other members of our senior management team. The loss of services of any of these individuals, who all have at-will employment arrangements with us, could delay or prevent the successful development of our product pipeline, completion of our planned clinical trials or the commercialization of our product candidates.

Replacing key employees may be a difficult, costly and protracted process, and we may not have other personnel with the capacity to assume all 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 us, and a history of successful development and commercialization. If we cannot attract and retain skilled personnel, as needed, we may not achieve our development and other goals.

In addition, the success of our business will depend 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 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 do not have, and do not have plans to establish commercial manufacturing facilities. We completely rely on third parties for the manufacture and supply of our clinical trial drug and delivery device supplies and, if approved, commercial product materials. The loss of any of these vendors or a vendor's failure to provide us with an adequate supply of clinical trial or commercial product material in a timely manner and on commercially acceptable terms, or at all, could harm our business.

We outsource the manufacture of our product candidates and do not plan to establish our own manufacturing facilities. To manufacture our product candidates, we have made numerous custom modifications at contract manufacturing organizations ("CMOs"), making us highly dependent on these CMOs. For clinical and commercial supplies, if approved, we have supply agreements with third-party CMOs for drug substance, finished drug product, drug delivery devices and other necessary components of our product candidates. While we have secured long-term commercial supply agreements with many of the third-party CMOs, we would need to negotiate agreements for commercial supply with several important CMOs, and we may not be able to reach agreement on acceptable terms. In addition, we rely on these third parties to conduct or assist us in 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 their tasks successfully in a timely manner, whether for technical, financial or other reasons, we may be unable to secure clinical trial material, or commercial supply material if approved, which likely would delay the initiation, conduct or completion of our clinical studies or prevent us from having enough commercial supply material for sale, which would have a material and adverse effect on our business.

All manufacturers of our clinical trial material and, if approved, commercial product, including drug substance manufacturers, must comply with requirements for current good manufacturing practices ("cGMP") 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 and our representatives generally monitor and audit our manufacturers' systems, we do not have full control over their ongoing compliance with these regulations, and while the responsibility to maintain cGMP compliance is shared between us and the third-party manufacturer, we ultimately bear responsibility for our supply chain and compliance with regulatory standards. Failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay or failure to obtain product approval, product seizure or recall, or withdrawal of product approval.

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

Any new manufacturer or supplier of finished drug product or its component materials, including drug substance and delivery devices, 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 of such product or ingredients required by us. The FDA or foreign regulatory agency 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

the drug substance or drug product for future clinical trials or commercial product, the FDA or regulatory authorities outside of the U.S. may require us to conduct additional clinical and nonclinical studies to ensure comparability of the drug substance or drug product manufactured by our current CMOs to that manufactured by the new supplier. Changing of suppliers or equipment is particularly challenging for companies like us, with inhalation products, because any change could alter the performance of the drug product. For example, the manufacturing of the drug substance of Molgradex, molgramostim, a biological drug substance, as well as the drug product, Molgradex, may potentially be transferred to a new manufacturing site. Producing Molgradex, a biological product, is challenging, and therefore, may require more time and resources than previously anticipated. The transfer of the manufacturing to the new site may also cause regulatory agencies, including the FDA, to require additional nonclinical or clinical studies, which may cause delay or failure to obtain regulatory approval, and incur substantial additional cost.

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. Some of our product candidates have not 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. 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 and/or add expense.

If our manufacturers encounter any of the aforementioned difficulties or otherwise fail to comply with their contractual obligations or there are delays entering 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, Molgradex and AeroVanc are currently manufactured entirely or partially outside the U.S. and, as a result, we may experience interruptions in supply due to shipping or customs difficulties or regional instability. Furthermore, changes in currency fluctuations, shipping costs, or import tariffs could adversely affect cost of goods sold. 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 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, contract research organizations (“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 all or 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 their activities as required or expected including the maintenance of good clinical practice (“GCP”), GLP, and cGMP, compliance, which are ultimately our responsibility to ensure. Further, such third parties may not be as committed to the success of our programs as our own employees and, therefore, may not devote the same time, thoughtfulness or creativity to completing projects or problem-solving as our own employees would. 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 their programs. If our CROs, study investigators, and/or third-party sponsors fail to devote sufficient time and resources to studies of our product candidates, if we and/or our CROs do not comply with all GLP and GCP regulatory and contractual requirements, or if their performance is substandard, we 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.

In addition, CROs we engage may have relationships with other commercial entities, some of which may compete with us. Through intentional or unintentional means, our competitors may benefit from lessons learned on our projects that could ultimately harm our competitive position. Moreover, if a CRO fails to properly, or at all, perform our activities 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 before 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 and/or announced development timelines and have a material adverse impact on our business and financial condition.

We currently have limited marketing capabilities and no sales organization. If we are unable to establish sales and marketing capabilities on our own or through third parties, we will be unable to successfully commercialize our products, if approved, or generate product revenue.

To commercialize our products, if approved, in the U.S. and other jurisdictions we seek to enter, we must build our marketing, sales, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. If our products receive regulatory approval, we expect to market such products in the U.S. through a focused, specialized sales force, which will be costly and time consuming. Institutionally, we have no prior experience in the marketing and sale of pharmaceutical products, and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain and incentivize qualified individuals, identify sufficient patient leads, provide adequate training to sales and marketing personnel and effectively manage a geographically dispersed sales and marketing team. Outside of the U.S., we may consider collaboration arrangements. If we are unable to enter into such arrangements on acceptable terms or at all, we may not be able to successfully commercialize our products in certain markets. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of our products. If we are not successful in commercializing our products, either on our own or through collaborations with one or more third parties, our future product revenue will suffer and we would incur significant additional losses.

Any future acquisitions that we make could disrupt our business and harm our financial condition.

We expect to evaluate, from time to time, potential strategic acquisitions of complementary businesses, products or technologies. In addition, we expect to evaluate joint ventures, licensing and other collaborative projects. We may not be able to identify appropriate acquisition candidates or strategic partners, or successfully negotiate, finance or integrate acquisitions of any businesses, products or technologies. Furthermore, the integration of any acquisition and management of any collaborative project may divert our management's time and resources from our core business and disrupt our operations. Any cash acquisition we pursue would diminish the funds otherwise available to us for other uses. Any acquisition using our stock would dilute our stockholders' ownership interests.

To establish a sales and marketing infrastructure and expand our manufacturing capabilities, we will need to increase the size of our organization, and we may experience difficulties in managing this growth.

As of March 13, 2019, we had 33 full-time employees, including 23 employees engaged in research and development. As we advance our product candidates through the development process and to commercialization, we will need to continue to expand our development, regulatory, quality, managerial, sales and marketing, operational, finance and other resources to manage our operations and clinical trials, continue our development activities and commercialize our product candidates, if approved. As our operations expand, we expect that we will need to manage additional relationships with various manufacturers and collaborative partners, suppliers and other organizations.

Due to our limited financial resources and our limited experience in managing a company with anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. In addition, the physical expansion of our operations may lead to significant costs and may divert our management attention and resources. Any inability to manage growth could delay the execution of our development and strategic objectives, or disrupt our operations, which could materially impact our business, revenue and operating results.

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

Undesirable side effects or adverse events 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. A significant challenge in clinical development is that the patient population in early studies, where small numbers of patients are required, is different from the patient population observed in later stage studies, where larger groups of patients are required. For example, patients in earlier stage studies may be more sick, compliant, or otherwise motivated than patients in larger studies. As such, efficacy or safety results may differ significantly between studies. Side-effects seen at high doses in earlier studies of AeroVanc, such as bronchoconstriction or other airway irritation, may be seen in significant numbers at the lower doses selected for later studies. Also, for AeroVanc, while not observed in the Phase 2 clinical study, the emergence of vancomycin-resistant MRSA could occur during the longer dosing period of AeroVanc that is currently implemented in the Phase 3 clinical study. If this or other undesirable side effects occur, they could possibly prevent approval, which would have a material and adverse effect on our business.

If any of our product candidates receive marketing approval and we or others later identify undesirable side effects caused by the 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.

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 have announced.

We have set goals for accomplishing certain objectives material to the successful development of our product candidates. The actual timing of these events may vary 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 create 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 significant assumptions that may prove to be incorrect. 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. 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 costlier than anticipated, we may determine that the associated time and cost are not financially justifiable and, as a result, may discontinue development in a particular indication or of the product candidate as a whole. In addition, even if a study did complete with successful results, changes may occur in regulatory requirements or policy during the period of product development and/or regulatory review of an NDA or BLA that relate to the data required to be included in NDAs and BLAs which may require additional studies that may be costly and time consuming. Any of these actions may be viewed negatively, which could adversely impact our financial condition.

Further, throughout development, we must provide adequate assurance to the FDA and other regulatory authorities that we can consistently develop and produce our product candidates in conformance with GLP, GCP, 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 deficiencies 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 or failure of development or commercialization of our product candidates.

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 our standards, 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 them. The misconduct of our employees and other service providers could 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. Although we have adopted a code of business ethics and conduct, 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 them, 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. For example, if one of our manufacturing partners was placed under a consent decree, we may be hampered in our ability to manufacture clinical or commercial supplies.

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

We rely on information technology systems, including third-party "cloud based" service providers, to keep financial records, maintain laboratory, clinical data and corporate records, communicate with staff and external parties and operate other critical functions. This includes critical systems such as email, other communication tools, electronic document repositories, and archives. If any of these third-party information technology ("IT") providers are compromised due to computer viruses, unauthorized access, malware, natural disasters, fire, terrorism, war and telecommunication failures, electrical failures, cyber-attacks or cyber-intrusions over the internet, then sensitive emails or documents could be exposed or deleted. Similarly, we could incur business disruption if our access to the internet is compromised and we are unable to connect with third-party IT providers. 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, we rely on third parties to 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 a third-party IT provider's 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 or could fail. We have experienced and may continue to experience attempts to breach our security and attempt to introduce malicious software into our information technology systems; however, to date and to our knowledge, such attacks have not resulted in any material damage to us.

We are continually working to maintain reliable systems to control costs and improve our operations. Our efforts include, but are not limited to the following: firewalls, antivirus protection, patches, log monitors, routine backups with offsite retention of storage media, system audits, data partitioning and routine password modifications. Our internal information technology systems environment continues to evolve, and our business policies and internal security controls may not keep pace as new threats emerge. No assurance can be given that our efforts to continue to enhance our systems will be successful.

If we fail to comply with data protection laws and regulations, we could be subject to government enforcement actions (which could include civil or criminal penalties), private litigation and/or adverse publicity, which could negatively affect our operating results and business.

A number of state, national, and foreign laws and regulations apply to the collection, use, retention, protection, disclosure, transfer, and other processing of personal data. Due to our Danish subsidiary, Savara ApS, our clinical trial activities, and operations in Europe, we are subject to data protection laws in the EU, including the General Data Protection Regulation ("GDPR"). The GDPR, which became effective on May 25, 2018, has caused the EU requirements for the protection of personal data to become more stringent and increased the penalties for noncompliance. Penalties can consist of fines up to €20 million or 4% of global annual revenues, whichever is higher. As a result, we have been required to implement additional mechanisms to ensure compliance with the new EU data protection rules, which may cause us to incur additional costs.

If we or our vendors fail to comply with applicable data privacy laws, including the GDPR, we could be subject to government enforcement actions and significant penalties against us, and our business could be adversely impacted.

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

Our corporate headquarters is located in a single commercial facility in Austin, Texas, USA. We maintain a second office in a single commercial facility in Denmark where many of our product development staff are located. Important documents and records, including copies of our regulatory documents and other records for our product candidates, are located both at a secure offsite document storage facility as well at our own 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 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 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 any positive results in prior clinical studies do not ensure that ongoing or future clinical studies will be successful.

Pharmaceutical products are subject to stringent regulatory requirements covering quality, safety, and efficacy. The burden of proof is on the manufacturer, such as Savara, to show with substantial clinical data that the risk/benefit profile for any new drug is favorable. Only after successfully completing extensive pharmaceutical development, nonclinical testing, and clinical studies may a product be considered for regulatory approval.

Clinical studies are expensive and difficult to design and implement, they 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. There is significant risk in clinical development where later stage clinical studies are designed and powered based on the analysis of data from earlier studies, with these earlier studies involving a smaller number of patients, and the results of the earlier studies being driven primarily by a subset of responsive patients. 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 the sponsor company, resulting in delay or failure to obtain marketing approval for a product candidate. Additionally, the possible lack of standardization across multiple investigative sites may induce variability in the results, which can interfere with the evaluation of treatment effects.

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. Any safety or efficacy concern identified in a third-party sponsored study could adversely affect our or another licensee's development of our product candidates and prospects for regulatory approval, even if the data from that study are subject 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 us to 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. Failure to complete a clinical study of a product candidate or an unsuccessful result of a clinical study could have a material adverse effect on our business.

Molgradex and AeroVanc have received Orphan Drug Designation by the FDA and Molgradex has received Orphan Drug Designation also in Europe. While orphan designation provides certain benefits there are also associated risks.

Molgradex has received Orphan Drug Designation in the U.S. by the FDA and in Europe by the European Medicines Agency for the treatment of aPAP, and AeroVanc has been granted Orphan Drug Designation in the U.S. by the FDA for the treatment of MRSA lung infection in patients with CF. Orphan Drug Designation will not shorten the regulatory review or reduce the clinical data requirements needed to obtain approval. If approval is received to market either Molgradex or AeroVanc for the respective indications, FDA will not approve a similar product, with the same active ingredient, to Molgradex or AeroVanc for seven years and the European Medicines Agency will not approve a similar product to Molgradex for ten years, unless we are unable to produce enough supply to meet demand in the marketplace or another similar product, with the same active ingredient, is deemed clinically superior. Similar product candidates, with the same active ingredient and route of delivery, may be granted Orphan Drug Designation during the development of the respective products, but the Orphan Drug exclusivity is granted only to the first of such products approved, which means there is risk that a competitor product candidate may receive approval and Orphan Drug exclusivity before us, thus preventing us from marketing one or more of our product candidates until the exclusivity of the competing product expires. Also, the Orphan Drug status will not prevent a competitor with a different active ingredient from competing with our product candidates. If we are prevented from marketing one or more product candidates due to a competitor's Orphan Drug exclusivity, this would have a material adverse effect on our business.

Delays in commencement and completion of clinical studies are common and have many causes. Delays in clinical studies of our product candidates would likely 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 to initiate or continue a clinical study;
- delays in obtaining regulatory approval to commence a clinical study;
- delays in identifying and reaching agreement on acceptable terms with prospective CROs, clinical study sites and investigators, which agreements can be subject to extensive negotiation and may vary significantly among study sites;
- delays in obtaining regulatory approval in a prospective country;
- delays in obtaining ethic committee approval to conduct a clinical study at a prospective site;
- delays in reaching agreements on acceptable terms with prospective 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;
- geopolitical risks associated with CROs, CMOs, and other third-party vendors;

- delays in the production or delivery of sufficient quantities of clinical trial material or drug delivery devices from our CMOs and other vendors to initiate or continue a clinical study;
- delays due to product candidate recalls as result of stability failure, excessive product complaints or other failures of the product candidate during its use or testing;
- invalidation of clinical data caused by premature unblinding or integrity issues;
- invalidation of clinical data caused by mixing up of the active drug and placebo through randomization or manufacturing errors;
- 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, which historically can be challenging in orphan diseases;
- delays caused by patients dropping out of a clinical study due to side effects, concurrent disorders, difficulties in adhering to the study protocol, unknown issues related to different patient profiles than in previous studies, such as the reduced age limit required for inclusion into the AeroVanc Phase 3 study, or otherwise;
- delays in having patients complete participation in a clinical study, including returning for post-treatment follow-up;
    - delays resulting from study sites dropping out of a trial, providing inadequate staff support for the study, problems with shipment of study supplies to clinical sites or focusing its staff's efforts on enrolling studies that compete for the same patient population;
- 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 population, the proximity of patients to clinical sites, the eligibility criteria for the study, the design of the clinical study, ongoing studies competing for the same patient population and clinicians, patients' perceptions as to the potential advantages of the drug being studied in relation to available alternatives, including therapies being investigated by other companies which may be viewed as more beneficial or important to study, fear of being randomized to the placebo arm, and changes in standard of care. Challenges to complete enrollment can be exacerbated in orphan indications, like those being pursued by us, with a limited number of qualifying patients and the lack of clinical sites with the necessary expertise and experience to conduct our studies. Further, completion of a clinical study and/or its results may be adversely affected by failure to retain patients who enroll in a study but withdraw due to adverse side effects, perceived lack of efficacy, belief that they are on placebo, improvement in condition before treatment has been completed, or for personal reasons, or without reason, or by patients who fail to return for or complete post-treatment follow-up.

Clinical studies may not begin on time or be completed in the time frames we anticipate and may be costlier than we anticipate for a variety of reasons, including one or more of those described above. The length of time necessary to successfully 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. 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 candidates 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 ultimately commercialize our product candidates, the standard of care may have changed or other therapies for the same indications may have been introduced to the market in the interim and may establish a competitive threat to us or diminish the need for our products.

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 is generally very expensive, takes many years to complete and failures 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 exact funds required to complete research and development, obtain regulatory approval and commercialize all of our product candidates. We will need significant additional capital to continue to advance our products as per current business plans.

Failure at any 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.

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; and
- 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 re-examination and approval 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 may be required, and regulatory approval may be conditioned, delayed or denied, any of which could delay or prevent us from successfully marketing our product candidates and substantially harm our business.

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 materially 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.

Molgradex is currently undergoing a Phase 3 clinical study in the U.S., Europe, and Japan. Except for the drug product manufacturing site, the product (formulation, process, packaging, and device) used in this Phase 3 study will be submitted in marketing applications to regulatory authorities unchanged. However, the product submitted may result in regulatory delays and/or non-acceptance for a variety of reasons including but not limited to: justification for inclusion of one or more excipients; safety qualification of one or more excipients; acceptability of commercial manufacturing site; ease of presenting the dose to the nebulizer; and, reproducibility of the delivered dose from the nebulizer. Concurrently, we are exploring formulation, process, packaging, and device improvements that could simplify the composition of the drug product by eliminating one or more potentially unnecessary or harmful excipients, improve the ease of use of the product, and/or reduce the overall product variability. While we expect these changes to improve the product quality and possibly reduce other documentation requirements, the regulatory agencies may require additional clinical or nonclinical studies prior to approval of such changes, including conducting

an additional Phase 3 clinical study that would significantly extend the timeline for clinical development of Molgradex in aPAP.

The manufacturing process and site for the drug product may change post-Phase 3. Changes in the manufacturing process and site have a potential to result in untoward changes in drug product characteristics. If the commercial drug product differs significantly from the product studied in Phase 3, then regulatory agencies may require additional clinical or nonclinical studies prior to approval of such changes, including conducting an additional Phase 3 clinical study that would significantly extend the timeline for clinical development of Molgradex in aPAP.

We received guidance from the FDA on the requirements to initiate clinical studies in the U.S. and on the clinical study requirements to achieve BLA approval for Molgradex. Based on the guidance, we amended our ongoing Phase 3 clinical study to include more patients and amended our endpoint hierarchy and statistical analyses to be used for U.S. approval purposes. Even if the clinical study meets all of its statistical goals and protocol end points, the FDA may not view the results to provide persuasive evidence of efficacy across multiple clinical endpoints. Instead, they may require additional clinical studies and/or other costly studies, including an additional Phase 3 study, which would require us to expend substantial additional resources and would significantly extend the timeline for clinical development prior to market approval, or result in failure to complete the clinical development of Molgradex.

We have commenced the Phase 3 trial of AeroVanc, the success of which will be needed for FDA approval to market AeroVanc in the U.S. to treat persistent MRSA lung infection in individuals living with CF. While significant communication with the FDA on the Phase 3 study design has occurred, even if the Phase 3 clinical study meets all of its statistical goals and protocol end points, the FDA may not view the results as robust and convincing. They may require additional clinical studies and/or other costly studies, which could require us to expend substantial additional resources and could significantly extend the timeline for clinical development prior to market approval. Additionally, we are conducting a two-year nonclinical carcinogenicity study on the AeroVanc powder, required by the FDA. The results of this study will not be known until a short time prior to potential submission of an NDA or BLA for AeroVanc. If the carcinogenicity study cannot be completed for technical or other reasons or provides results that the FDA determines to be concerning, this may cause a delay or failure in obtaining approval for AeroVanc.

Significant uncertainty exists with respect to the regulatory approval process for any investigational new drug, including Molgradex, and AeroVanc. Regardless of any guidance the FDA or foreign regulatory agencies may provide a drug's sponsor during its development, the FDA or foreign regulatory agencies retain complete discretion in deciding whether to accept an NDA or BLA or the equivalent foreign regulatory approval submission for filing or, if accepted, approve an NDA or BLA. There are many components to an NDA or BLA or marketing authorization application submission in addition to clinical study data. For example, the FDA or foreign regulatory agencies will review the sponsor's internal systems and processes, as well as those of its CROs, CMOs and other vendors, related to development of its product candidates, including those pertaining to its clinical studies and manufacturing processes. Before accepting an NDA or BLA for review or before approving the NDA or BLA, the FDA or foreign regulatory agencies may request that we provide additional information that may require significant resources and time to generate and there is no guarantee that its product candidates will be approved for any indication for which we may apply. The FDA or foreign regulatory agencies may choose not to approve an NDA or BLA 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 candidates. 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 or foreign regulatory agencies 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 one or more 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 competitors may bring products to market before us, which could impair our ability to generate revenues from the product candidates, or even seek approval, if blocked by a competitor's Orphan Drug exclusivity, which would have a material adverse effect on 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, a U.S. federal government shut-down or budget sequestration, such as one that occurred during January 2018 and December 2018 through January 2019, may result in significant reductions to the FDA's resources, employees and operations, which may lead to slower response times and longer review periods, potentially affecting our ability to progress development of our product candidates or obtain regulatory approval for our product candidates.

Even if the FDA or foreign regulatory agencies grant approvals for our product candidates, the conditions or scope of the approval(s) may limit successful commercialization of the product candidates and impair our ability to generate substantial sales revenue. For example, the FDA may approve label claims for AeroVanc with age restrictions and/or treatment duration limitations, or Molgradex with restrictions for use only by patients unresponsive to the current standard of care. They may limit the label of Molgradex or AeroVanc to a subset of patients based on a review of which patient groups had the greatest efficacious response in clinical studies. Such label restriction may be undesirable and may limit successful commercialization. The FDA or foreign regulatory agencies may also only grant marketing approval contingent on the performance of costly post-approval nonclinical or clinical studies, or subject to warnings or contraindications that limit commercialization. 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 cGMP, GCP, international conference on harmonization regulations and GLP, which are regulations and guidelines that are enforced by the FDA or foreign regulatory agencies for all of its clinical development and for any clinical studies that we conduct post-approval. The FDA or foreign regulatory agencies 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 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, implement risk minimization procedures, and/or conduct post-approval studies, which in turn could result in significant expense and delay or limit our ability to generate sales revenues.

Regulations may be changed prior to submission of a marketing application that require higher hurdles than currently anticipated. These may occur as a result of drug scandals, recalls, or a political environment unrelated to our products.

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

Even if initial regulatory approval is obtained, 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;
- 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 payers, the revenue we generate from its sales will be limited and our business may never achieve profitability.

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 payers, including government payers. 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 products as demonstrated in clinical studies;
- acceptance in the medical and patient communities of our products as a safe and effective treatment;
- the product's taste, ease of use, or features associated with the delivery device;
- 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 a product's approved labeling;
- reimbursement and coverage policies of government and other third-party payers;
- pricing and cost-effectiveness of our product relative to alternative treatments;
- availability of alternative treatments;

- smaller than expected market size due to lack of disease awareness of a rare disease, or the patient population with a specific rare disease being smaller than anticipated;
- inappropriate diagnostic efforts due to limited knowledge and/or resources among clinicians;
- 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 approved. 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 payers 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 expenditures 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 products outside of the U.S., we must establish and comply with the 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 generally differs from that required to obtain FDA approval. The regulatory approval process in other countries may include all of the risks 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. Conversely, if the product candidates do receive approval outside the U.S. in the future, we may not meet the FDA requirements in the U.S. for approval.

We must comply with the U.S. Foreign Corrupt Practices Act and similar foreign anti-corruption laws.

The U.S. Foreign Corrupt Practices Act, to which we are subject, prohibits corporations and individuals from engaging in certain activities to obtain or retain business or to influence a person working in an official capacity. It is illegal to pay, offer to pay or authorize the payment of anything of value to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. Other countries, such as the U.K., have similar laws with which we must comply. We face the risk that an employee or agent could be accused of violating one or more of these laws, particularly in geographies where significant overlap exists between local government and healthcare industries. Such an accusation, even if unwarranted, could prove disruptive to our developmental and commercialization efforts.

Risks Related to Our Intellectual Property

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

AeroVanc has received a U.S. Patent Notice of Allowance for its formulation in the U.S., AeroVanc's primary market. AeroVanc has either been issued patents or is prosecuting patent applications in numerous countries outside the U.S. We have no patent protection for Molgradex for the treatment of aPAP, and primarily rely on the Orphan Drug exclusivity as our primary barrier to competition. Molgradex for the treatment of NTM has issued patents ex-U.S. (under prosecution in the U.S.) with an additional international patent application pending. Both Molgradex and AeroVanc utilize proprietary delivery devices with exclusive supply agreements. Molgradex is eligible for protection via a proprietary cell bank used in the production of the drug substance.

Our success will depend on our ability to:

- obtain and maintain patent and other exclusivity rights with respect to our products and their uses;
- 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 U.S. and, after March 15, 2013, in the U.S. In addition, changes in or different interpretations of patent laws in the U.S. 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.

Our AeroVanc patent is specific to the formulation of the AeroVanc powder. While this may prevent identical products from entering the market, it may not preclude someone skilled in the art from inventing an alternate formulation approach with comparable or improved characteristics.

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 results of operations. For Molgradex, which is administered via nebulization, we may rely on regulatory exclusivity for the combination of Molgradex and its delivery system. However, there is no assurance that our Molgradex 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. We intend to seek approval for new names for AeroVanc and Molgradex that meet the FDA's and foreign regulatory requirements. 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 proposed or approved 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. For example, we filed a trademark for the name "Savara" and were challenged. We decided to terminate its application, but we may revisit such filings at a future date. Further, our competitors may infringe our trademarks or we may not have adequate resources to enforce our trademarks.

Our success depends 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.

We have filed for patent protection in the U.S. and other countries to cover the formulation of AeroVanc and were granted a notice of allowance in the U.S., its primary market. However, this patent may not provide us with significant competitive advantages, because the validity or enforceability of the 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 re-examination, 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, or courts. 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 us before and after our patents expire.

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 Molgradex for treating NTM lung infection. Because the potential use and potential therapeutic benefits of systemically administered GM-CSF for systemic NTM disease have been described in case reports in the literature, the use of an inhaled form of GM-CSF may be considered to lack novelty and an inventive step, and therefore be unpatentable.

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 our best interests. We or any future licensors or licensees may 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 U.S. 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 use our patents 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 once Orphan Drug and Qualified Infectious Disease Product exclusivities have expired. See the section entitled “Risks Related to Our Industry” for further description of Orphan Drug and Qualified Infectious Disease Product exclusivities.

Enforcement of intellectual property rights in certain countries outside the U.S. 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 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 United States Patent and Trademark Office ("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. If we fail to comply with these requirements, it may 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 its patent 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. 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 our 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 our 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 our 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 management's time and attention from our 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;
- 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.

There may be issued or filed 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. Additionally, such patents may be issued or filed in the future. 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.

In the future, we may need to enforce our proprietary rights, or to determine the scope, validity and enforceability 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 competition in the marketplace for our product candidates, should any of them receive regulatory approval.

Molgradex and AeroVanc have received Orphan Drug Designation from the FDA and Molgradex has received Orphan Drug Designation from the European Medicines Agency. Orphan Drug Designation will provide market exclusivity in the U.S. for 7 years and 10 years in Europe, but only if (1) Molgradex and AeroVanc receive market approval before a competitor using the same active compound for the same indication, (2) we are able produce sufficient supply to meet demand in the marketplace, and (3) another product with the same active ingredient is not deemed clinically superior. AeroVanc has also received Qualified Infectious Disease Product ("QIDP") status extending market exclusivity by an additional five years in addition to any other exclusivity obtained in the U.S.

The industries in which we operate (biopharmaceutical, specialty pharmaceutical, biotechnology and pharmaceutical) are highly competitive and subject to rapid and significant change. 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 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 us, 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. These advantages may enable them to receive approval from the FDA or any foreign regulatory agency before us and prevent us from competing due to their orphan drug protections. 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, easier to dose, 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 payer 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 on the extent to which the costs of such products will be covered by third-party payers, such as government health programs, commercial insurance and other organizations. Third-party payers 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. These challenges to prices may be problematic to us since our products are targeted for a small number of patients (those suffering from orphan diseases) thus requiring us to charge very high prices in order to recover development costs and achieve a profit on our revenue. If these third-party payers do not consider our products to be cost-effective compared to other therapies, we may not obtain coverage for our products after approval as a benefit under the third-party payers' plans or, even if we do, the level of coverage or payment may not be sufficient to allow us to sell our products on a profitable basis.

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 payers in the U.S., therefore coverage and reimbursement for drug products can differ significantly

from payer to payer. 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 payer separately, with no assurance that coverage and adequate payment will be applied consistently or obtained. The process for determining whether a payer 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 payer reimbursement to providers of our products, if approved, may be subject to a bundled payment that also includes the procedure of administering our products or third-party payers may require providers to perform additional patient testing to justify the use of 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 governments, 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 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 worldwide 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 and President Trump has stated that reducing drug pricing is a priority for his administration. We expect that federal, state and local governments in the U.S., as well as in other countries, 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 payers 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, especially in light of our plans to price our product candidates at a high level.

Furthermore, we cannot predict that healthcare reform measures that may be adopted in the future, and the potential impact of any such measures on our operations and financial position is uncertain, but may result in more rigorous coverage criteria, lower reimbursement, and additional downward pressure on the price we may receive for approved product. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products, if approved.

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 or involved in the use of 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;
- 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 for 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, if judgments exceed our insurance coverage, could consume a significant portion of our cash and adversely affect our business.

Risks Related to our Common Stock

Our stock price is expected to continue to be volatile.

The market price of our common stock has been and is expected to continue to be subject to significant fluctuations. Market prices for securities of early-stage pharmaceutical, biotechnology and other life sciences companies have historically been particularly volatile. Some of the factors that may cause the market price of our common stock to fluctuate include:

- our ability to obtain regulatory approvals for our product candidates, and delays or failures to obtain such approvals;
- failure to meet or exceed any financial and development projections that we may provide to the public;
- failure to meet or exceed the financial and development projections of the investment community;
- failure of any of our product candidates, if approved, to achieve commercial success;
- failure to maintain our existing third-party license and supply agreements;
- failure by us or our licensors to prosecute, maintain, or enforce our intellectual property rights;
- changes in laws or regulations applicable to our product candidates;
- any inability to obtain adequate supply of our product candidates or the inability to do so at acceptable prices;
- adverse regulatory authority decisions;
- introduction of new products, services, or technologies by our competitors;
- if securities or industry analysts do not publish research or reports about our business, or if they issue adverse or misleading opinions regarding our business and stock;
- failure to obtain sufficient capital to fund our business objectives;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;
- the perception of the pharmaceutical industry by the public, legislatures, regulators, and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures, or capital commitments by us or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- additions or departures of key personnel;
- significant lawsuits, including patent or stockholder litigation;
- changes in the market valuations of similar companies;
- general market or macroeconomic conditions;
- announcements by commercial partners or competitors of new commercial products, clinical progress or the lack thereof, significant contracts, commercial relationships or capital commitments;
- adverse publicity relating to the CF, aPAP or NTM markets generally, including with respect to other products and potential products in such markets;
- the introduction of technological innovations or new therapies that compete with potential products of the combined organization;
- changes in the structure of health care payment systems; and
- period-to-period fluctuations in our financial results.

Moreover, the stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies. These broad market fluctuations may also adversely affect the trading price of our common stock.

In the past, following periods of volatility in the market price of a company’s securities, stockholders have often instituted class action securities litigation against those companies. Such litigation, if instituted, could result in substantial costs and diversion of management attention and resources, which could significantly harm our profitability and reputation.

We continue to incur costs and demands upon management as a result of complying with the laws and regulations affecting public companies.

We will continue to incur significant legal, accounting and other expenses associated with public company reporting requirements. We will also continue to incur costs associated with corporate governance requirements, including requirements under the Sarbanes-Oxley Act, as well as rules implemented by the SEC and Nasdaq. These rules and regulations may increase our legal and financial compliance costs and to make some activities more time-consuming and costly. For example, our management team consists of certain officers prior to the Merger whom have not previously managed and operated a public company. These officers and other personnel will need to devote substantial time to gaining expertise regarding operations as a public company and compliance with applicable laws and regulations. These rules and regulations may also make it difficult and expensive for us to obtain directors' and officers' liability insurance. As a result, it may be more difficult for us to attract and retain qualified individuals to serve on our board of directors or as executive officers, which may adversely affect investor confidence in us and cause our business or stock price to suffer.

We do not expect to pay any cash dividends in the foreseeable future.

We expect to retain any future earnings to fund the development and growth of our business. As a result, capital appreciation, if any, of our common stock will be stockholders' sole source of gain, if any, for the foreseeable future.

Because the Merger likely has resulted in an ownership change under Section 382 of the Internal Revenue Code, our pre-Merger net operating loss carryforwards and certain other tax attributes will be subject to limitation. The net operating loss carryforwards and certain other tax attributes may also be subject to limitations as a result of ownership changes.

If a corporation undergoes an "ownership change" within the meaning of Sections 381, 382, and 383 of the Internal Revenue Code, the corporation's net operating loss carryforwards and certain other tax attributes arising from before the ownership change are subject to limitations on use after the ownership change. In general, an ownership change occurs if there is a cumulative change in the corporation's equity ownership by certain stockholders that exceeds fifty percentage points over a rolling three-year period. Similar rules may apply under state tax laws. The Merger resulted in an ownership change for us and, accordingly, our net operating loss carryforwards and certain other tax attributes with respect to the pre-closing period will be subject to limitations on use. Additional ownership changes in the future could result in additional limitations on our net operating loss carryforwards. Consequently, even if we achieve profitability, we may not be able to utilize a material portion of our net operating loss carryforwards and other tax attributes, which could have a material adverse effect on cash flow and results of operations.

Item 1B. Unresolved Staff Comments.

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

Item 2. Properties.

Effective January 1, 2018, we relocated our corporate headquarters within Austin, Texas, where we sublease approximately 6,151 square feet of office space pursuant to a sublease that expires in 2021.

We believe that our existing facilities are adequate for our near-term needs. When our existing lease expires, we may look for alternate space for our operations. We believe that suitable alternative space would be available on commercially reasonable terms if required in the future.

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 and administrative 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 on the Nasdaq Global Select Market under the ticker symbol "SVRA."

As of March 11, 2019, we had approximately 137 record holders of our common stock. The number of beneficial owners is substantially greater than the number of record holders because a large portion of our common stock is held of record through brokerage firms in "street name."

Unregistered Sales of Equity Securities

On December 4, 2018, in connection with entering into an amendment to our Loan and Security Agreement with Silicon Valley Bank ("SVB") dated April 28, 2017 and previously amended on October 31, 2017, we issued two warrants (the "SVB Warrants") to SVB and its affiliate Life Science Loans II, LLC, pursuant to which SVB and Life Science Loans II, LLC may each purchase up to 5,666 shares of Savara's common stock, par value $0.001 per share, subject to adjustment in accordance with the terms of the SVB Warrants, for a per share exercise price of $8.824. The SVB Warrants expire on December 4, 2028.

In issuing the SVB Warrants, we relied on the private offering exemption of Section 4(a)(2) of the Securities Act of 1933, as amended, based on the following factors: (i) the absence of general solicitation; (ii) investment representations obtained from SVB and Life Science Loans II, LLC, including representations with respect to their status as accredited investors; (iii) the provision of appropriate disclosure; and (iv) the placement of restrictive legends on the issued warrants.

Item 6. Selected Financial Data.

Not applicable.

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

Savara Inc. is an orphan lung disease company. Our pipeline comprises Molgradex, an inhaled granulocyte-macrophage colony-stimulating factor ("GM-CSF") in Phase 3 development for autoimmune pulmonary alveolar proteinosis ("aPAP"), in Phase 2a development for nontuberculous mycobacterial ("NTM") lung infection, and in preparation for Phase 2a development in cystic fibrosis ("CF") affected individuals with chronic NTM lung infection, and AeroVanc, a Phase 3 stage inhaled vancomycin for treatment of persistent methicillin-resistant Staphylococcus aureus ("MRSA") lung infection in individuals living with CF. Our strategy involves expanding our pipeline of potentially best-in-class products through indication expansion, strategic development partnerships and product acquisitions, with the goal of becoming a leading company in our field. Our management team has significant experience in orphan drug development and pulmonary medicine, in identifying unmet needs, developing and acquiring new product candidates, and effectively advancing them to approval and commercialization.

Savara and our wholly-owned subsidiaries, including Aravas Inc., Savara ApS, Drugrecure A/S, and Savara Australia Pty. Limited operate in one segment with our principal offices in Austin, Texas. Since inception, we have devoted substantially all of our efforts and resources to identifying and developing our product candidates, recruiting personnel, and raising capital. We have incurred operating losses and negative cash flow from operations and have no material product revenue from inception to date. From inception to December 31, 2018, we have raised net cash proceeds of approximately $209.3 million, primarily from public offerings of our common stock, private placements of convertible preferred stock, and debt financings.

We have never been profitable and have incurred operating losses in each year since inception. Our net losses were $61.5 million and $29.8 million for the years ended December 31, 2018 and 2017, respectively. As of December 31, 2018, we had an accumulated deficit of $129.7 million. Substantially all of our operating losses resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations.

We have chosen to operate by outsourcing our manufacturing and most of our clinical operations. We expect to incur significant additional expenses and increase our operating losses for at least the next several years as we initiate and continue the clinical development of, and seek regulatory approval for, our product candidates and add necessary personnel accordingly. We expect that our operating losses will fluctuate significantly from quarter to quarter and year to year due to timing of clinical development programs and efforts to achieve regulatory approval.

As of December 31, 2018, we had cash and cash equivalents of $24.3 million and short-term investments of $86.5 million. We will continue to require substantial additional capital to continue our clinical development and potential commercialization activities. Accordingly, we will need to raise substantial additional capital to continue to fund our operations. The amount and timing of our future funding requirements will depend on many factors, including the pace and results of our clinical development efforts. Failure to raise capital as and when needed, on favorable terms or at all, would have a negative impact on our financial condition and our ability to develop our product candidates.

Merger with Mast Therapeutics, Inc.

On April 27, 2017, we completed our business combination with Mast Therapeutics, Inc. (“Mast”), a publicly held company, in accordance with the terms of the Agreement and Plan of Merger and Reorganization (the “Merger Agreement”), dated January 6, 2017 (the “Merger”) (refer to Note 1 of the consolidated financial statements in this report). In connection with and immediately prior to the effective time of the Merger, Mast implemented a reverse stock split at a ratio of one new share for every 70 shares of its common stock outstanding. Under the terms of the Merger Agreement, each outstanding share of Savara common stock was then converted into Mast common stock at a ratio of approximately .5860 of a Savara share (the “Exchange Ratio”). As a result of the Merger, the Mast equity holders owned approximately 23% of the combined company, and Savara’s pre-existing equity holders owned approximately 77%. In connection with the Merger, Mast changed its name to Savara Inc.

2017 Comprehensive Tax Reform

In December 2017, the U.S. government enacted comprehensive tax legislation that includes significant changes to the taxation of business entities. These changes include, among others, (i) a reduction to the corporate income tax rate, (ii) a partial limitation on the deductibility of business interest expense, (iii) a shift of the U.S. taxation of multinational corporations from a tax on worldwide income to a territorial system (along with certain rules designed to prevent erosion of the U.S. income tax base) and (iv) a one-time tax on accumulated offshore earnings held in cash and illiquid assets, with the latter taxed at a lower rate.

Further, the newly enacted comprehensive tax legislation, among other things, reduces the orphan drug credit from 50% to 25% of qualifying expenditures. When and if we become profitable, this reduction in tax credits may result in an increased federal income tax burden on our orphan drug programs as it may cause us to pay federal income taxes earlier under the revised tax law than under the prior law and, despite being partially off-set by a reduction in the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, may increase our total federal tax liability attributable to such programs.

Notwithstanding the reduction in the corporate income tax rate, the overall impact of this tax reform is uncertain, and our business and financial condition could be adversely affected.

Critical Accounting Policies and Estimates

Our management’s discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the U.S. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses. On an ongoing basis, we evaluate these estimates and judgments. We base our estimates on historical experience and on various assumptions that we believe to be reasonable under the circumstances. These estimates and assumptions form the basis for making judgments about the carrying values of assets and liabilities and the recording of expenses that are not readily apparent from other sources. Actual results may differ materially from these estimates. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management’s judgments and estimates.

Accrued Research and Development Expenses

We record accrued expenses for estimated costs of our research and development activities conducted by external service providers, which include the conduct of clinical trials and contract formulation and manufacturing activities. We record the estimated costs of development activities based upon the estimated amount of services provided but not yet invoiced, and include these costs in accrued liabilities in the consolidated balance sheet and within development expense in the consolidated statement of operations and comprehensive loss. These costs are a significant component of our research and development expenses. We record accrued expenses for these costs based on the estimated amount of work completed and in accordance with agreements established with these external service providers.

We estimate the amount of work completed through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fee to be paid for such services. We make significant judgments and estimates in determining the accrued balance in each reporting period. As actual costs become known, we adjust our accrued estimates.

Business Combinations

We account for business combinations, such as our acquisitions of Serendex in July 2016 and Mast in April 2017, in accordance with Accounting Standards Codification ("ASC") Topic 805, "Business Combinations," and as further defined by Accounting Standards Update ("ASU") 2017-01, "Business Combinations (Topic 805)" 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.

ASU 2017-04, "Intangibles-Goodwill and Other (Topic 350): Simplifying the Test for Goodwill Impairment," provides an impairment model providing the Company the option to implement a one-step method for determining impairment of goodwill thereby simplifying the subsequent measurement of goodwill by eliminating Step 2 (measuring a goodwill impairment loss by comparing the implied fair value of a reporting unit's goodwill with the carrying amount of that goodwill) from the goodwill impairment test. Under the amendments in this guidance, an entity should perform its annual, or interim, goodwill impairment test by comparing the fair value of a reporting unit with its carrying amount. An entity should recognize an impairment charge for the amount by which the carrying amount exceeds the reporting unit's fair value; however, the loss recognized should not exceed the total amount of goodwill allocated to that reporting unit. Additionally, an entity should consider income tax effects from any tax deductible goodwill on the carrying amount of the reporting unit when measuring the goodwill impairment loss, if applicable.

With respect to the impairment testing of acquired IPR&D, ASU 2011-08, "Intangibles – Goodwill and Other (Topic 350): Testing Goodwill for Impairment," and ASU 2012-02, "Intangibles – Goodwill and Other (Topic 350): Testing Indefinite-Lived Intangible Assets for Impairment," provides us a two-step impairment process with 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 acquired IPR&D is impaired. If we choose to first assess qualitative factors and we determine that it is more-likely-than not acquired IPR&D is not impaired, we are not required to take further action to test for impairment.

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, the Multi-Period Excess Earnings Method, ("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. In evaluating potential impairment of our acquired Molgradex IPR&D as of September 30, 2018, we utilized a qualitative approach and determined it was more-likely-than not that the fair value was not

impaired. In evaluating potential impairment of our acquired Molgradex goodwill as of June 30, 2018, performed the quantitative analysis based upon market capitalization and no impairment to goodwill was noted. While we continue to evaluate opportunities to monetize our acquired assets, we can provide no assurances that we will be able to do so. However, we believe that our approach is a more appropriate method for assessing fair value in the context of our current business.

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.

During the first quarter of 2018, we recorded $21.7 million of impairment charges and a corresponding decrease to the carrying value of IPR&D related to the Aironite drug candidate assumed in the Merger (as defined and discussed further under Note 7 of the consolidated financial statements in this report) due to the unfavorable results from a Phase 2 study that demonstrated a failure of Aironite to meet the endpoints of the study and limited effectiveness of the compound in patients. As a result of the IPR&D impairment charges recorded in the first quarter of 2018, the Company reduced the associated deferred tax liability related to the acquired IPR&D from the Merger by $4.6 million and recorded an income tax benefit.

Share-based Compensation Expenses

We recognize the cost of stock-based awards granted to employees based on the estimated grant-date fair value of the awards. The value of the portion of the award that is ultimately expected to vest is recognized as expense ratably over the requisite service period. We recognize the compensation costs for awards that vest over several years on a straight-line basis over the vesting period. Forfeitures are recognized when they occur, which may result in the reversal of compensation costs in subsequent periods as the forfeitures arise. We recognize the cost of stock-based awards granted to non-employees at their then-current fair values as services are performed, and such awards are remeasured through the counterparty performance date.

We estimate the grant-date fair value of a stock option award using the Black-Scholes option pricing model ("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.

Revenue

We record revenue based on a five-step model in accordance with ASC 606, "Revenue from Contracts with Customers." To date, we have not generated any product revenue from our product candidates.

Milestone Revenue

With respect to our license agreement as discussed further under Note 16 of the consolidated financial statements in this report, which includes certain milestone payments to be remunerated to us by the licensee, we identify the performance obligations, determine the transaction price, allocate the contract transaction price to the performance obligations, and recognize the revenue when (or as) the performance obligation is satisfied. We identify the performance obligations included within the license agreement and evaluate which performance obligations are distinct.

The milestone payments are a form of variable consideration as the payments are contingent upon achievement of a substantive event. The milestone payments are estimated and included in the transaction price when we determine, under the variable consideration constraint, that it is probable that there will not be a significant reversal of cumulative revenue recognized in future periods. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achievement of such milestones and any related constraint, and if necessary, adjust the estimate of the overall transaction price.

Grants and Awards

To date, we have recognized revenue solely from federal grants under the Small Business Innovation Research Program of the Department of Health and Human Services, National Institutes of Health, and an award from the Cystic Fibrosis Foundation, a non-profit organization, as further described in Note 13 of the consolidated financial statements in this report. We record revenue related to the federal grants as qualifying costs are incurred, and when there is reasonable assurance that the performance conditions of the grant have been met and the grant will be received. We record revenue related to an award from the Cystic Fibrosis Foundation upon completion and achievement of defined milestones, and when there is reasonable assurance that the performance conditions of the award have been met and collectability is reasonably assured.

Income Taxes

We use the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the carrying amounts and the tax basis of assets and liabilities. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect of a change in tax rates on deferred tax assets and liabilities will be recognized in the period that includes the enactment date. A valuation allowance is established against the deferred tax assets to reduce their carrying value to an amount that is more-likely-than not to be realized.

Financial Operations Overview

Research and Development Expenses

We recognize all research and development expenses as they are incurred. These expenses consist primarily of the following:

- expenses incurred under agreements with consultants and clinical trial sites that conduct research and development activities on our behalf;
- laboratory and vendor expenses related to the execution of our clinical trials;
- contract manufacturing expenses, primarily for the production of clinical supplies; and
- internal costs that are associated with activities performed by our research and development organization and generally benefit multiple programs. Where appropriate, these costs are allocated by product candidate. Unallocated internal research and development costs consist primarily of:
- personnel costs, which include salaries, benefits and stock-based compensation expense;
- allocated facilities and other expenses, which include expenses for rent and maintenance of facilities and depreciation expense; and
- regulatory expenses and technology license fees related to development activities.

The largest component of our operating expenses has historically been our investment in research and development activities. The following table shows our research and development expenses by product candidate for the years ended December 31, 2018 and 2017:

	Year ended December 31,	
	2018	2017
	(In thousands)	
Product candidates:		
Molgradex	$19,796	$10,352
AeroVanc	15,565	7,181
Other	1,812	979
Total research and development expenses	$37,173	$18,512

We expect research and development expenses will increase in the future as we advance our product candidates into and through clinical trials and pursue regulatory approvals, which will require a significant increased investment in regulatory support and contract manufacturing and inventory build-up related costs. In addition, we continue to evaluate opportunities to acquire or in-license other product candidates and technologies, which may result in higher research and development expenses due to license fee and/or milestone payments.

The process of conducting clinical trials necessary to obtain regulatory approval is costly and time consuming. We may never succeed in timely developing and achieving regulatory approval for our product candidates. The probability of success of our product candidates may be affected by numerous factors, including clinical data, competition, intellectual property rights, manufacturing capability and commercial viability. As a result, we are unable to accurately determine the duration and completion costs of our development projects or when and to what extent we will generate revenue from the commercialization and sale of any of our product candidates.

General and Administrative Expenses

General and administrative, or G&A, expenses primarily consist of salaries, benefits, 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 G&A expenses include facility lease and insurance costs.

Other Income/(Expense), Net

Other income/(expense) includes: (i) interest payments made and interest expense related to debt issuance costs and debt discount under our amended loan agreement with Silicon Valley Bank, (ii) interest expense associated with payments under capital leases of equipment, and (iii) interest accrued on the 2016 Notes and 2017 Notes up to the Merger date. Interest expense is typically reported net of interest income which includes interest earned on our cash, cash equivalent and short-term investment balances. Other income/(expense) also includes net unrealized and realized gains and losses from foreign currency transactions, foreign exchange derivatives not designated as hedging, and securities subject to fair value accounting as well as any other non-operating gains and losses.

Results of Operations — Comparison of Years Ended December 31, 2018 and 2017

	Year ended December 31,		Dollar Change
	2018	2017	
	(in thousands)		
Operating expenses:			
Research and development	$37,173	$18,512	$18,661
General and administrative	10,654	11,081	(427)
Impairment of acquired IPR&D	21,692	—	21,692
Depreciation	526	363	163
Total operating expenses	70,045	29,956	40,089
Loss from operations	(70,045)	(29,956)	(40,089)
Other income (expense)	18	(3,475)	3,493
Net loss before income taxes	(70,027)	(33,431)	(36,596)
Income tax benefit	8,511	3,634	4,877
Net loss	$(61,516)	$(29,797)	$(31,719)

Research and development

Research and development expenses increased by $18.7 million, or 100.8%, to $37.2 million for the year ended December 31, 2018 from $18.5 million for the year ended December 31, 2017. The increase was primarily due to $9.4 million in increased development costs associated with the development of Molgradex, including the expansion of the aPAP study in the U.S. and the commencement of the NTM study, an increase of $8.4 million in AeroVanc study costs related to Phase 3 activities, and $1.0 million in expense in the form of our common stock issued to Cardeas in connection with our acquisition of its assets, which was expensed in the second quarter of 2018.

General and administrative

General and administrative expenses decreased by $0.4 million, or 3.9%, to $10.7 million for the year ended December 31, 2018 from $11.1 million for the year ended December 31, 2017. The decrease was primarily due to $2.0 million of additional expense in connection with the change in fair value of the contingent consideration associated with the Serendex Acquisition recognized during the year ended December 31, 2017 versus the related expense incurred for the year ended December 31, 2018, as offset by increased noncash stock-based compensation charges of approximately $1.8 million, as well as other expenditures associated with public company requirements and other general and administrative activities, recognized in the year ended December 31, 2018 versus the year ended

December 31, 2017.

Impairment of IPR&D

During the year ended December 31, 2018, we recognized a $21.7 million impairment charge to the carrying value of IPR&D related to the Aironite drug candidate assumed in the Merger due to the unfavorable results from a Phase 2 study that demonstrated a failure of Aironite to meet the endpoints of the study and limited effectiveness of the compound in patients. We are no longer supporting or pursuing the Aironite drug candidate.

Other income / (expense)

Other expense decreased by $3.5 million for the year ended December 31, 2018 compared to the year ended December 31, 2017. During the year ended December 31, 2017, we recognized $2.0 million of expense associated with the extinguishment of certain pre-Merger convertible promissory notes and related put option liabilities which were subsequently extinguished or converted to common stock as part of the Merger in 2017. The decrease in other expense was also the result of certain activities incurred during the year ended December 31, 2018, including an increase of approximately $1.4 million in interest and accretion income earned on short-term investments recognized as we only had short-term investments outstanding for a limited duration during the year ended December 31, 2017.

Income tax benefit

Income tax benefit increased by $4.9 million, or 134.2%, to $8.5 million for the year ended December 31, 2018 from $3.6 million for the year ended December 31, 2017. The increase was primarily due to a $4.6 million tax benefit recorded during the first quarter of 2018 related to the reversal of a deferred tax liability resulting from the impairment of IPR&D acquired in the Merger.

Liquidity and Capital Resources

Sources of Liquidity

Since inception through December 31, 2018, our operations have been financed primarily by net cash proceeds of approximately $209.3 million, primarily from public offerings of common stock, private placements of convertible preferred stock, and debt financings. As of December 31, 2018, we had $24.3 million in cash, $86.5 million in short-term investments, and an accumulated deficit of $129.7 million. We expect that our research and development and general and administrative expenses will increase, and, as a result, we anticipate that we will continue to incur increasing losses in the foreseeable future. Therefore, we will need to raise additional capital to fund our operations, which may be through the issuance of additional equity and potentially through borrowings.

Debt Facility

On April 28, 2017 we entered into a loan and security agreement with Silicon Valley Bank, as amended on October 31, 2017 (the “Loan Agreement”), which provided for a $15.0 million credit facility that was made available in two equal tranches. In December 2018, the Company entered into an amendment to the Loan Agreement (the “Amendment”) to increase the amount of the term loan facility from $15.0 million to $45.0 million and make certain other changes. The Loan Agreement, as amended by the Amendment, provides that the funds are available in two tranches, (i) $25.0 million became available upon the effectiveness of the Amendment, of which $15.0 million was used to refinance the existing amount outstanding under the loan facility, and (ii) $20.0 million is to be made available upon the our request prior to September 30, 2019, subject to certain conditions. However, if we draw the second tranche, it will be required

to provide cash collateral for $20.0 million if our market cap falls below $200.0 million, until certain market cap requirements and thresholds are met.

Silicon Valley Bank has been granted a perfected first priority lien in all of our assets with a negative pledge on our intellectual property. The Loan Agreement contains customary affirmative and negative covenants, including among others, covenants limiting our ability and our subsidiaries to dispose of assets, permit a change in control, merge or consolidate, make acquisitions, incur indebtedness, grant liens, make investments, make certain restricted payments and enter into transactions with affiliates, in each case subject to certain exceptions.

Following the Amendment, the loans bear interest at the prime rate reported in The Wall Street Journal, plus a spread of 3.0% (reduced from 4.25%). Interest only payments are due through October 2020 followed by monthly payments of principal plus interest over the following 25 months and a maturity date of November 1, 2022. The Loan Agreement, as amended by the Amendment, will also require (i) a prepayment fee (3.0% of funded amounts in months 1-12, 2.0% of funded amounts in months 13-24, and 1.0% thereafter); and (ii) end of term charge equal to 6.0% of the amount of principal borrowed. In connection with the Amendment, Savara paid Silicon Valley Bank a $0.6 million end of term payment fee, and the prepayment penalty contemplated by the Loan Agreement was abated. Upon execution of the Amendment, Silicon Valley Bank advanced us an additional $10.0 million, net legal costs and $0.6 million for the end of term payment pursuant to the terms of the Loan Agreement, as partially abated pursuant to the Amendment, to fully fund the amount of the first tranche under the Amendment. As of December 31, 2018, we have not drawn any funds from the second tranche under the Amendment.

The capital is being utilized to fund our ongoing development programs and for general corporate purposes.

Common Stock Sales Agreement

On April 28, 2017, we entered into a Common Stock Sales Agreement with H.C. Wainwright & Co., LLC ("Wainwright"), as sales agent, which was amended by Amendment No. 1 to the Common Stock Agreement (the "Amendment") on June 29, 2018 (the "Sales Agreement"), pursuant to which we may offer and sell, from time to time, through Wainwright, shares of our common stock, par value $0.001 per share (the "Shares"), having an aggregate offering price of not more than $60.0 million, in addition to the $2.3 million in shares sold prior to the Amendment. The Amendment was effective on July 13, 2018, at the time our Registration Statement on Form S-3, dated June 29, 2018, (the "New Registration Statement") was declared effective by the Securities and Exchange Commission. The Shares will be offered and sold pursuant to the New Registration Statement. Subject to the terms and conditions of the Sales Agreement, Wainwright will use its commercially reasonable efforts to sell the Shares from time to time, based upon our instructions. We have provided Wainwright with customary indemnification rights, and Wainwright will be entitled to a commission at a fixed commission rate equal to 3.0% of the gross proceeds per Share sold. Sales of the Shares, if any, under the Sales Agreement may be made in transactions that are deemed to be "at the market offerings" as defined in Rule 415 under the Securities Act of 1933, as amended. We have no obligation to sell any of the Shares and may at any time suspend sales under the Sales Agreement or terminate the Sales Agreement.

During the years ended December 31, 2018 and 2017, we sold 48,600 shares and 198,298 shares of common stock under the Sales Agreement for net proceeds of approximately $0.5 million and $1.7 million, respectively.

Public Offerings

On June 7, 2017, we completed an underwritten public offering consisting of 9,034,210 shares of our common stock, which included 613,157 shares upon the partial exercise of the underwriters' option to purchase additional shares of our common stock at the public offering price. The net proceeds from the offering, after deducting the underwriting discounts and commissions and offering expenses, were approximately $39.5 million. The public offering was executed under an existing shelf registration statement as previously filed with the Securities and Exchange Commission on August 12, 2015 and declared effective on August 19, 2015.

On October 27, 2017, we completed an underwritten public offering consisting of 6,037,500 shares of our common stock, which included 787,500 shares upon the exercise of the underwriters' option to purchase additional shares of our common stock at the public offering price and pre-funded warrants to purchase 775,000 shares of our common stock. The net proceeds from the offering, after deducting the underwriting discounts and commissions and offering expenses, were approximately $50.0 million. The public offering was executed under an existing shelf registration statement as previously filed with the Securities and Exchange Commission on August 12, 2015 and declared effective on August 19, 2015.

On July 30, 2018, we completed an underwritten public offering consisting of 4,250,000 shares of our common stock at a price to the public of $11.50 per share. The net proceeds from the offering, after deducting the underwriting discounts and commissions and offering expenses, were approximately $45.8 million. The July 2018 public offering was executed under the New Registration Statement.

We have used and intend to use the net proceeds from these offerings for working capital and general corporate purposes, which include, but are not limited to, the funding of clinical development of and pursuing regulatory approval for our product candidates, the initiation of Molgradex pre-commercialization activities, and general and administrative expenses.

Cash Flows

The following table summarizes our cash flows for the periods indicated:

	Year ended December 31,	
	2018	2017
	(in thousands)	
Cash used in operating activities	$(39,275)	$(28,234)
Cash used in investing activities	(13,619)	(69,115)
Cash provided by financing activities	55,193	106,089
Effect of exchange rate changes	(119)	8
Net increase in cash	$2,180	$8,748

Cash flows from operating activities

Cash used in operating activities for the year ended December 31, 2018 was $39.3 million, consisting of a net loss of $61.5 million, which was partially offset by non-cash charges of $19.8 million, mainly comprised of impairment of IPR&D, depreciation, non-cash interest, fair value changes, provision for deferred taxes, accretion on discount to short-term investments, amortization of debt issuance costs, and stock-based compensation, and increased by a net increase in assets and liabilities of $2.4 million. The change in our net operating assets and liabilities was primarily due to an increase in accrued liabilities mostly related to research and development costs for both AeroVanc and Molgradex.

Cash used in operating activities for the year ended December 31, 2017 was $28.2 million, consisting of a net loss of $29.8 million, which was partially offset by noncash charges, net of deferred tax benefit, of $3.6 million, mainly comprised of depreciation, noncash interest, fair value changes, loss on debt extinguishment, accretion of discount to convertible promissory notes, and stock-based compensation, and by a net decrease in assets and liabilities of $2.0 million. The change in our net operating assets and liabilities was primarily due to an increase in prepaid assets mostly related to research and development costs for Molgradex and AeroVanc.

Cash flows from investing activities

Cash used in investing activities for the year ended December 31, 2018 was primarily the result of net purchases of short-term investments.

Cash used in investing activities for the year ended December 31, 2017 was the result of cash used to purchase available-for-sale securities partially offset by the cash acquired related to the Merger and maturities of available-for-sale securities.

Cash flows from financing activities

Cash provided by financing activities for the year ended December 31, 2018 was primarily related to net proceeds of $45.8 million from a public offering of 4,250,000 shares of our common stock completed on July 30, 2018, $0.5 million from the “at the market offering” under the Sales Agreement, and net increase of $9.4 million from our Loan Agreement, as revised by the Amendment, as partially offset by $0.5 million in principal payments on our capital lease obligation.

Cash provided by financing activities for the year ended December 31, 2017 was primarily related to proceeds from the issuance of $89.6 million of common stock net of issuance costs, $11.3 million in net proceeds from our debt facility, $3.6 million related to proceeds from the issuance of a convertible promissory note and $1.7 million from the “at the market offering” under the Sales Agreement, net of issuance costs.

Future Funding Requirements

We have not generated any revenue from product sales. We do not know when, or if, we will generate any revenue from product sales. We do not expect to generate any revenue from product sales unless and until we obtain regulatory approval for and commercialize any of our product candidates. At the same time, we expect our expenses to increase in connection with our ongoing development and manufacturing activities, particularly as we continue the research,

development, manufacture and clinical trials of, and seeking of regulatory approval for, our product candidates. In addition, subject to obtaining regulatory approval of any of our product candidates, we anticipate that we will need substantial additional funding in connection with our continuing operations.

As of December 31, 2018, we had cash, cash equivalents, and short-term investments of $110.8 million. We will continue to require substantial additional capital to continue our clinical development and potential commercialization activities. Accordingly, we will need to raise substantial additional capital to continue to fund our operations. The amount and timing of our future funding requirements will depend on many factors, including the pace and results of our clinical development efforts. Failure to raise capital as and when needed, on favorable terms or at all, would have a negative impact on our financial condition and our ability to develop our product candidates.

Until we can generate a sufficient amount of product revenue to finance our cash requirements, we expect to finance our future cash needs primarily through the issuance of additional equity and potentially through borrowings, grants and strategic alliances with partner companies. To the extent that we raise additional capital through the issuance of additional equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of existing stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant rights to develop and market product candidates to third parties that we would otherwise prefer to develop and market ourselves.

License and Royalty Agreements

We are also subject to certain contingent payments to the Cystic Fibrosis Foundation ("CFF") in connection with a grant award. In September 2013, we received a $1.7 million award ("CFF Award") from CFF. The CFF Award includes disbursements to us based on the achievement of certain milestones. We are subject to certain royalty payments due to CFF under the CFF Award based on commercialization of our product, AeroVanc, and either the achievement of certain sales volumes or a change in control transaction, as defined below.

Commercial Approval Royalty

A royalty is payable to the CFF equal to three (3) times the amount of the CFF Award upon approval of our product for commercial use. The royalty is payable in equal installments of 33% due 60 days after first commercial sale; 33% due within 90 days of the first anniversary of the first commercial sale; and 34% due within 90 days of second anniversary of the first commercial sale. This royalty will be reduced upon change in control transaction payments as described below or a sale or license of the AeroVanc program with a third party but not to exceed an amount equal to three (3) times the CFF Award. As our product, AeroVanc, has not yet been approved for commercial use, we have not recorded a liability for the commercial approval royalty.

Additional Royalties

In addition, if net sales exceed $50.0 million for any calendar year occurring during the first five years after the first commercial sale, we must remit payment to the CFF equal to one (1) times the CFF Award. Furthermore, if net sales exceed $100.0 million for any calendar year occurring during the first five years after first commercial sale, we must remit an additional payment to the CFF equal to one (1) times the CFF Award. Given that we have not recognized any sales from our product, we have not recorded a liability for any amounts due as additional royalties.

Change in Control Royalty

Upon a change in control transaction, as defined below, occurring prior to the second anniversary date of the effective date of the CFF Award at September 30, 2015, we must remit a royalty payment to the CFF equal to 5% of the proceeds from the change in control transaction but not to exceed an amount equal to two (2) times the CFF Award proceeds received. Upon a change in control transaction occurring after the second anniversary date of the effective date of the CFF Award, we must remit a royalty payment to the CFF equal to 5% of the proceeds from the change in control transaction but not to exceed an amount equal to three (3) times the CFF Award.

A change in control transaction is defined as the consummation (in a single or series of transactions) of a (i) merger, share exchange, or other reorganization; (ii) sale by one or more stockholders of a majority voting power; or (iii) sale of substantially all of our assets. We have determined that a change of control is not probable and as such, have not recorded a liability for the change in control royalty.

The CFF Award may not be assigned by any party (other than to an affiliate or to a successor to substantially all of such party's assets or business to which the CFF Award relates) without the consent of the other party.

If we initiate an "Interruption," as defined under the CFF Award, for more than one year at any time before the first commercial sale of the product under the AeroVanc Program, we may cease to conduct, or have ceased to use commercially reasonable efforts to advance the research and development or commercialization of the AeroVanc program, we shall transfer an exclusive, worldwide license to the CFF of our research and development of the product under the AeroVanc program limited to the right to manufacture, have manufactured, license, sell, use, support, offer to sell, any related invention from our AeroVanc program.

Amendment

On November 28, 2017, we entered into an amendment agreement, effective September 30, 2017, to the CFF Award ("Amended CFF Award"), pursuant to which the amount of the development award available to us was increased by $5.0 million to an aggregate of $6.7 million. Pursuant to the terms of the Amended CFF Award, if we elect to draw down funds on the increased award, we are obligated to make royalty payments to CFF upon the commercialization of AeroVanc.

A payment equal to four (4) times the amount we receive under the Amended CFF Award is due in three installments: 33% due 60 days after first commercial sale of AeroVanc; 33% due within 90 days after the first anniversary of the first commercial sale of AeroVanc; and 34% due within 90 days after the second anniversary of the first commercial sale of AeroVanc. Additionally, if net sales of AeroVanc exceed $50.0 million for any calendar year occurring during the first five years after the first commercial sale of AeroVanc, we must remit payment to CFF equal to the amount received by us under the Amended CFF Award. Furthermore, if net sales exceed $100.0 million for any calendar year occurring during the first seven years after first commercial sale of AeroVanc, we must remit an additional payment to CFF equal to the amount received by us under the Amended CFF Award. We are also obligated to make royalty payments to CFF if we enter into a change of control transaction or a sale or license of the AeroVanc program with a third party equal to 7.5% of the amount received from the third party in connection with such transaction, up to a total of four (4) times the amount received by us under the Amended CFF Award. Any such payments are to be credited against the royalty payments due upon commercialization of AeroVanc, and we must continue paying or cause the third party to assume any remaining royalties payable to CFF pursuant to the Amended CFF Award.

As of December 31, 2018 and 2017, we had drawn down $1.7 million, in total, under the CFF Award dated September 2013 but made no draws against the Amended CFF award.

Manufacturing and Other Commitments and Contingencies

We are subject to various manufacturing royalties and payments and other commitments related to our product candidate, Molgradex.

For a summary of the contingent milestone payments and commitments, refer to Note 2, “Summary of Significant Accounting Policies - Manufacturing Commitments and Contingencies,” of the consolidated financial statements in this report.

Other Contracts

We enter into contracts in the normal course of business with various third parties for research studies, clinical trials, testing and other services. These contracts generally provide for termination upon notice, and therefore we believe that our non-cancelable obligations under these agreements are not material.

Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet arrangements and do not have any holdings in variable interest entities.

Management Outlook

Recent Accounting Pronouncements

See Note 2, “Summary of Significant Accounting Policies - Recent Accounting Pronouncements,” of the 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 short-term investment securities. Such interest-earning instruments carry a degree of interest rate risk; however, we have not been exposed to nor do we anticipate being exposed to material risks due to changes in interest rates. A hypothetical 1% change in interest rates

during any of the periods presented would not have had a material impact on our audited consolidated financial statements. Additionally, our investment securities are fixed income instruments denominated and payable in U.S. dollars and have short-term maturities, typically less than twelve months, and typically carry credit ratings of “A” at a minimum by two of three nationally recognized statistical rating organizations, specifically Moody’s, Standard & Poor’s or Fitch. As such, we do not believe that our cash, cash equivalents and short-term investment securities have significant risk of default or illiquidity.

We have ongoing operations in Denmark as a result of our Serendex Acquisition and pay those vendors in local currency (Danish Krone) or Euros. We seek to limit the impact of foreign currency fluctuations through the use of derivative instruments, and short-term foreign currency forward exchange contracts not designated as hedging instruments. We did not recognize any significant exchange rate losses during the years ended December 31, 2018 and 2017. A 10% change in the Krone-to-dollar or Euro-to-dollar exchange rate on December 31, 2018 would not have had a material effect on our results of operations or financial condition.

We also have interest rate exposure as a result of our Loan Agreement, as amended, with SVB. As of December 31, 2018, the outstanding gross principal amount of the secured term loan was $25.0 million. The loan bears interest at the prime rate reported in The Wall Street Journal, plus a spread of 3.00%. 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, 2018 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.

Evaluation of Disclosure Controls and Procedures

Our management has evaluated, under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer, the effectiveness of our disclosure controls and procedures as of December 31, 2018, pursuant to and as required by Rule 13a-15(b) under the Exchange Act. Based on that evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of December 31, 2018, the Company's disclosure controls and procedures, as defined by Rule 13a-15(e) under the Exchange Act, were effective and designed to ensure that (i) information required to be disclosed in the Company's reports filed or submitted under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and (ii) information is accumulated and communicated to management, including the Chief Executive Officer and Chief Financial Officer, as appropriate to allow timely decisions regarding required disclosures.

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 Chief Executive Officer and Chief Financial Officer, we assessed the effectiveness of our internal control over financial reporting based on the framework in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (“COSO”). As a result of that assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2018 based on criteria in Internal Control - Integrated Framework (2013) issued by the COSO. The effectiveness of our internal control over financial reporting as of December 31, 2018 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report which appears in Item 15 of this Annual Report on Form 10-K.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during Savara's quarter ended December 31, 2018 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

Not applicable.

PART III

Certain information required by Part III of this report is omitted from this report pursuant to General Instruction G(3) of Form 10-K because we will file a definitive proxy statement pursuant to Regulation 14A for our 2019 annual meeting of stockholders (the "Proxy Statement") not later than 120 days after the end of the fiscal year covered by this report, and the information included in the Proxy Statement that is required by Part III of this report is incorporated herein by reference.

Item 10. Directors, Executive Officers and Corporate Governance.

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.savarapharma.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.

The other information required by this item will be set forth in the Proxy Statement and is incorporated into this report by reference.

Item 11. Executive Compensation.

The information required by this item will be set forth in the Proxy Statement and is incorporated into this report by reference.

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

The information required by this item will be set forth in the Proxy Statement and is incorporated into this report by reference.

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

The information required by this item will be set forth in the Proxy Statement and is incorporated into this report by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this item will be set forth in the Proxy Statement and is incorporated into this report by reference.

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 report of PricewaterhouseCoopers LLP and financial statements:

- Report of Independent Registered Public Accounting Firm on Financial Statements and Internal Control over Financial Reporting.
- Consolidated Balance Sheets as of December 31, 2018 and 2017.
- Consolidated Statements of Operations and Comprehensive Loss for the years ended December 31, 2018 and 2017.
- Consolidated Statements of Changes in Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit) for the years ended December 31, 2018 and 2017.
- Consolidated Statements of Cash Flows for the years ended December 31, 2018 and 2017.
- 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

Not applicable

Exhibit Index

2.1	Agreement and Plan of Merger and Reorganization, dated January 6, 2017, by and among the Registrant, Aravas Inc. (formerly Savara Inc.) and Victoria Merger Corp. (Incorporated by reference to Exhibit 2.1 to the Registrant's Current Report on Form 8-K filed on January 9, 2017.)
2.2	Business Transfer Agreement, dated May 13, 2016, between Aravas Inc. (formerly Savara Inc.) and Serendex Pharmaceuticals A/S (Incorporated by reference to Exhibit 2.6 to the Registrant's Registration Statement on Form S-4 filed on February 10, 2017.)
3.1	Amended and Restated Certificate of Incorporation, as amended, of the Registrant (Incorporated by reference to Exhibit 3.1 to the Registrant's Registration Statement on Form S-3 filed on June 29, 2018.)
3.2	Composite Amended and Restated Bylaws, as amended, of the Registrant (Incorporated by reference to Exhibit 3.2 to the Registrant's Annual Report on Form 10-K filed on March 26, 2014.)
4.1	Form of common stock certificate of the Registrant (Incorporated by reference to Exhibit 4.1 to the Registrant's Annual Report on Form 10-K filed on March 14, 2018.)
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 (Incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K filed on June 17, 2013.)
4.3	Form of Warrant Agent Agreement, dated as of November 6, 2014, between the Registrant and American Stock Transfer & Trust Company, LLC (Incorporated by reference to Exhibit 4.3 to the Registrant's Current Report on Form 8-K filed on November 7, 2014.)
4.4	Form of Warrant issued by the Registrant on November 12, 2014 (Incorporated by reference to Exhibit 4.4 to the Registrant's Current Report on Form 8-K filed on November 7, 2014.)
4.5	Warrant Agreement, dated as of August 11, 2015, between the Registrant and Hercules Technology III, L.P. (Incorporated by reference to Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q filed on November 12, 2015.)
4.6	First Amendment to Warrant Agreement, dated as of September 28, 2015, between the Registrant and Hercules Technology III, L.P. (Incorporated by reference to Exhibit 10.4 to the Registrant's Quarterly Report on Form 10-Q filed on November 12, 2015.)
4.7	Second Amendment to Warrant Agreement, dated as of February 25, 2016, between the Registrant and Hercules Technology III, L.P. (Incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K filed on February 29, 2016.)
4.8	Third Amendment to Warrant Agreement, dated as of March 3, 2017, between the registrant and Hercules Technology III, L.P. (Incorporated by reference to Exhibit 4.8 to the Registrant's Annual Report on Form 10-K filed on March 6, 2017.)
4.9	Form of Warrant Agreement entered into on February 16, 2016 between the Registrant and American Stock Transfer & Trust Company, LLC (Incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K filed on February 11, 2016.)
4.10	Form of Warrant Certificate for warrants to acquire common stock of the Registrant issued by the Registrant on February 16, 2016 (Incorporated by reference to Exhibit 4.2 to the Registrant's Current Report on Form 8-K filed on February 11, 2016.)
4.11	Form of Stock Purchase Warrant first issued by Aravas Inc. (formerly Savara Inc.) on July 15, 2016 (Incorporated by reference to Exhibit 4.11 to the Registrant's Registration Statement on Form S-4 filed on February 10, 2017.)
4.12	Warrant to Purchase Shares of Common Stock of the Registrant issued to Life Science Loans II, LLC on April 28, 2017 (Incorporated by reference to Exhibit 4.3 to the Registrant's Quarterly Report on Form 10-Q filed on May 5, 2017.)
4.13	Warrant to Purchase Shares of Common Stock of the Registrant issued to Silicon Valley Bank on April 28, 2017 (Incorporated by reference to Exhibit 4.2 to the Registrant's Quarterly Report on Form 10-Q filed on May 5, 2017.)

4.14	Amendment to Warrant to Purchase Shares of Common Stock of the Registrant issued to Life Science Loans II, LLC on June 26, 2017. (Incorporated by reference to Exhibit 4.1 to the Registrant's Quarterly Report on Form 10-Q filed on August 9, 2017.)

4.15		Amendment to Warrant to Purchase Shares of Common Stock of the Registrant issued to SVB Financial Group on June 26, 2017. (Incorporated by reference to Exhibit 4.2 to the Registrant's Quarterly Report on Form 10-Q filed on August 9, 2017.)
4.16		Warrant to Purchase Shares of Common Stock of the Registrant issued to Life Science Loans II, LLC on June 26, 2017. (Incorporated by reference to Exhibit 4.3 to the Registrant's Quarterly Report on Form 10-Q filed on August 9, 2017.)
4.17		Warrant to Purchase Shares of Common Stock of the Registrant issued to Silicon Valley Bank on June 26, 2017. (Incorporated by reference to Exhibit 4.4 to the Registrant's Quarterly Report on Form 10-Q filed on August 9, 2017.)
4.18		Form of Pre-Funded Warrant (Incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K filed on October 25, 2017.)
4.19		Warrant to Purchase Shares of Common Stock of the Registrant issued to Life Science Loans II, LLC on December 4, 2018.
4.20		Warrant to Purchase Shares of Common Stock of the Registrant issued to Silicon Valley Bank on December 4, 2018.
10.1		Common Stock Sales Agreement, dated April 28, 2017, between Savara Inc. and H.C. Wainwright & Co., LLC (Incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K filed on April 28, 2017.)
10.2		Loan and Security Agreement, dated April 28, 2017, among Savara Inc., Aravas Inc. and Silicon Valley Bank (Incorporated by reference to Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q filed on May 5, 2017.)
10.3		First Amendment, dated October 31, 2017, to Loan and Security Agreement, dated April 28, 2017, among Savara Inc., Aravas Inc. and Silicon Valley Bank. (Incorporated by reference to Exhibit 10.4 to the Registrant's Quarterly Report on Form 10-Q filed on November 8, 2017.)
10.4	#	Savara Inc. 2015 Omnibus Incentive Plan, as amended and restated (Incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed on June 7, 2018.)
10.5	#	Form of Non-Statutory Stock Option Grant Agreement—Director (for grants to non-employee directors) under the 2015 Omnibus Incentive Plan (Incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K filed on June 16, 2015.)
10.6	#	Form of Incentive Stock Option Grant Agreement – Exempt Employees under the 2015 Omnibus Incentive Plan (Incorporated by reference to Exhibit 10.3 to the Registrant's Current Report on Form 8-K filed on June 16, 2015.)
10.7	#	Form of Incentive Stock Option Grant Agreement – Non-Exempt Employees under the 2015 Omnibus Incentive Plan (Incorporated by reference to Exhibit 10.4 to the Registrant's Current Report on Form 8-K filed on June 16, 2015.)
10.8	#	Form of Non-Statutory Stock Option Grant Agreement – General under the 2015 Omnibus Incentive Plan (Incorporated by reference to Exhibit 10.8 to the Registrant's Annual Report on Form 10-K filed on March 14, 2018.)
10.9	#	Form of Incentive Stock Option Grant Agreement – Exempt Employees, in accordance with Danish employment law, under the 2015 Omnibus Incentive Plan. (Incorporated by reference to Exhibit 10.9 to the Registrant's Annual Report on Form 10-K filed on March 14, 2018.)
10.10	#	Form of Grant of Restricted Stock Units under the 2015 Omnibus Incentive Plan. (Incorporated by reference to Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q filed on November 8, 2017.)
10.11	#	Aravas Inc. (formerly Savara Inc.) Stock Option Plan (Incorporated by reference to Exhibit 10.53 to the Registrant's Registration Statement on Form S-4 filed on February 10, 2017.)
10.12	#	Aravas Inc. (formerly Savara Inc.) Form of Incentive Stock Option Agreement (Incorporated by reference to Exhibit 10.54 to the Registrant's Registration Statement on Form S-4 filed on February 10, 2017.)
10.11	#	Executive Employment Agreement, dated March 9, 2017, between Aravas Inc. (formerly Savara Inc.) and Robert Neville (Incorporated by reference to Exhibit 10.56 to Amendment No. 1 to the Registrant's Registration Statement on Form S-4 filed on March 13, 2017.)
10.12	#	

Executive Employment Agreement, dated March 9, 2017, between Aravas Inc. (formerly Savara Inc.) and Taneli Jouhikainen (Incorporated by reference to Exhibit 10.57 to Amendment No. 1 to the Registrant's Registration Statement on Form S-4 filed on March 13, 2017.)

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10.13#	Executive Employment Agreement, dated March 9, 2017, between Aravas Inc. (formerly Savara Inc.) and David Lowrance (Incorporated by reference to Exhibit 10.58 to Amendment No. 1 to the Registrant's Registration Statement on Form S-4 filed on March 13, 2017.)
10.14#	Form of Director and Officer Indemnification Agreement (Incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K filed on October 23, 2006.)
10.15+	Supply Agreement, dated September 26, 2016, between Aravas Inc. (formerly Savara Inc.) and Xellia Pharmaceuticals ApS (Incorporated by reference to Exhibit 10.59 to Amendment No. 1 to the Registrant's Registration Statement on Form S-4 filed on March 13, 2017.)
10.16+	Supply Agreement, effective September 1, 2012, between Aravas Inc. (formerly Savara Inc.) and Plastiape SpA, as amended by Amendment No. 1, dated June 1, 2016 (Incorporated by reference to Exhibit 10.60 to Amendment No. 1 to the Registrant's Registration Statement on Form S-4 filed on March 13, 2017.)
10.17+	Supply and Licensing Agreement, dated December 10th, 2012, and Addendum to Supply and License Agreement, dated February 22, 2016, between Savara Inc. and GEMA Biotech S.A. (Incorporated by reference to Exhibit 10.61 to Amendment No. 1 to the Registrant's Registration Statement on Form S-4 filed on March 13, 2017.)
10.18	Second Addendum, dated September 20, 2017, to the Supply and License Agreement, dated December 10, 2012, between Gemabiotech SAU and Savara ApS (Incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q filed on November 8, 2017.)
10.19+	Commercial Supply Agreement dated April 24, 2015 between PARI Pharma GmbH and Serendex Pharmaceuticals A/S (Incorporated by reference to Exhibit 10.62 to the Registrant's Registration Statement on Form S-4 filed on February 10, 2017.)
10.20+	Research Collaboration and License Agreement dated November 7, 2014 between PARI Pharma GmbH and Serendex Pharmaceuticals A/S (Incorporated by reference to Exhibit 10.63 to the Registrant's Registration Statement on Form S-4 filed on February 10, 2017.)
10.21	Sublease Agreement between Savara Inc. and Clubessential, LLC dated November 28, 2017 (Incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed on December 4, 2017.)
10.22	Sublease Agreement between Savara Inc. and Clubessential, LLC dated November 28, 2017 (Incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K filed on December 4, 2017.)
10.23	Settlement Agreement between Savara Inc. and Serenova A/S dated September 1, 2017 (Incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q filed on November 8, 2017.)
10.24	Research Program Award Letter Agreement between Savara Inc. and Cystic Fibrosis Foundation Therapeutics, Inc. dated September 30, 2013, as amended by Amendment No. 1, effective September 30, 2017 (Incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed on November 30, 2017.)
10.25	Sublease Agreement by and between the registrant and Santarus, Inc., effective as of June 19, 2014 (Incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed on June 30, 2014.)
10.26	Amendment No. 1 to Common Stock Sales Agreement, dated June 29, 2018, between Savara Inc. and H.C. Wainwright & Co., LLC. (Incorporated by reference to Exhibit 10.2 of the Registrant's Current Report on Form 8-K filed on June 29, 2018.)
10.27+	Amendment No. 1, effective May 23, 2018, to the Research Collaboration and License Agreement between Savara Inc. (as successor in interest to Serendex Pharmaceuticals A/S) and PARI Pharma GmbH dated November 7, 2014 (Incorporated by reference to Exhibit 10.3 of the Registrant's Quarterly Report on Form 10-Q filed on August 9, 2018.)
10.28#	Amendment to Executive Employment Agreement, dated as of August 3, 2018, by and among Savara Inc. and Taneli Jouhikainen (Incorporated by reference to Exhibit 10.4 of the Registrant's Quarterly Report on Form 10-Q filed on August 9, 2018.)
10.29#	Amendment to Executive Employment Agreement, dated as of August 3, 2018, by and among Savara Inc. and Dave Lowrance (Incorporated by reference to Exhibit 10.5 of the Registrant's Quarterly Report on Form 10-Q filed on August 9, 2018.)

10.30	#	Amendment to Executive Employment Agreement, dated as of August 3, 2018, by and among Savara Inc. and Robert Neville (Incorporated by reference to Exhibit 10.6 of the Registrant's Quarterly Report on Form 10-Q filed on August 9, 2018.)
10.31		Second Amendment, dated December 4, 2018, to Loan and Security Agreement, dated April 28, 2017, as amended on October 31, 2017, among Savara Inc., Aravas Inc. and Silicon Valley Bank.
21.1		List of Subsidiaries (Incorporated by reference to Exhibit 21.1 of the Registrant's Annual Report 10-K filed on March 14, 2018.)
23.1		Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm
24.1		Power of Attorney included on page 68 of this Form 10-K
31.1		Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a)
31.2		Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a)
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

# Indicates management contract or compensatory plan

+ Indicates that confidential treatment has been granted to certain portions of this exhibit, which portions have been omitted and filed separately with the SEC

** 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.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

Savara Inc.

Date: March 13, 2019 By: /s/ Robert Neville
Robert Neville
Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Robert Neville and Dave Lowrance, and each of them acting individually, as his attorney-in-fact, each with full power of substitution, for him in any and all capacities, to sign any and all amendments to this Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming our signatures as they may be signed by our said attorney to any and all amendments to said Report.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Robert Neville Robert Neville	Chief Executive Officer and Director (Principal Executive Officer)	March 13, 2019
/s/ Dave Lowrance Dave Lowrance	Chief Financial Officer (Principal Financial and Accounting Officer)	March 13, 2019
/s/ David Ramsay David Ramsay	Director	March 13, 2019
/s/ Matthew Pauls Matthew Pauls	Director	March 13, 2019
/s/ Joseph McCracken Joseph McCracken	Director	March 13, 2019

/s/ Nevan Elam Nevan Elam	Director	March 13, 2019
/s/ Rick Hawkins Rick Hawkins	Director	March 13, 2019
/s/ Yuri Pikover Yuri Pikover	Director	March 13, 2019

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Savara Inc.

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of Savara Inc. and its subsidiaries (the “Company”) as of December 31, 2018 and 2017, and the related consolidated statements of operations and comprehensive loss, of changes in redeemable convertible preferred stock and stockholders’ equity (deficit), and of cash flows for the years then ended, including the related notes (collectively referred to as the “consolidated financial statements”). We also have audited the Company's internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control - Integrated Framework (2013) issued by the COSO.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Report on Internal Control Over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on the Company’s consolidated financial statements and on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. 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 audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control over Financial Reporting

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 (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) 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 (iii) 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.

/s/ PricewaterhouseCoopers LLP
Austin, Texas
March 13, 2019

We have served as the Company's auditor since 2015.

Savara Inc. and Subsidiaries

Consolidated Balance Sheets

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

	As of December 31,	
	2018	2017
Assets		
Current assets:		
Cash and cash equivalents	$24,301	$22,121
Short-term investments	86,529	72,192
Prepaid expenses and other current assets	2,514	3,551
Total current assets	113,344	97,864
Property and equipment, net	522	925
In-process R&D	11,372	33,626
Goodwill	26,918	27,082
Other non-current assets	131	131
Total assets	$152,287	$159,628
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$3,879	$2,784
Accrued expenses and other current liabilities	3,334	2,966
Current portion of capital lease obligation	41	265
Total current liabilities	7,254	6,015
Long-term liabilities:		
Debt facility	24,530	14,775
Contingent consideration	12,214	11,948
Deferred tax liability	—	7,181
Capital lease obligation, net of current portion	—	297
Other long-term liabilities	70	103
Total liabilities	44,068	40,319
Stockholders' equity:		
Common stock, $0.001 par value, 200,000,000 and 500,000,000 shares authorized as of December 31, 2018 and 2017, respectively; 35,146,096 and 30,509,522 shares issued and outstanding as of December 31, 2018 and 2017, respectively	36	32
Additional paid-in capital	237,702	186,522
Accumulated other comprehensive income	200	958
Accumulated deficit	(129,719)	(68,203)
Total stockholders' equity	108,219	119,309
Total liabilities and stockholders' equity	$152,287	$159,628

The accompanying notes are an integral part of these consolidated financial statements.

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Savara Inc. and Subsidiaries

Consolidated Statements of Operations and Comprehensive Loss

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

	Years ended December 31,	
	2018	2017
Operating expenses:		
Research and development	$37,173	$18,512
General and administrative	10,654	11,081
Impairment of acquired IPR&D	21,692	—
Depreciation	526	363
Total operating expenses	70,045	29,956
Loss from operations	(70,045)	(29,956)
Other income (expense):		
Interest income (expense), net	11	(1,161)
Foreign currency exchange gain (loss)	71	(218)
Loss on extinguishment of debt	—	(1,816)
Change in fair value of financial instruments	(64)	(280)
Total other income (expense)	18	(3,475)
Loss before income taxes	(70,027)	(33,431)
Income tax benefit	8,511	3,634
Net loss	$(61,516)	$(29,797)
Accretion of redeemable convertible preferred stock	—	(578)
Deemed dividend on beneficial conversion feature	—	(404)
Net loss attributable to common stockholders	$(61,516)	$(30,779)
Net loss per share:		
Basic and diluted	$(1.85)	$(1.76)
Weighted-average common shares outstanding		
Basic and diluted	33,300,704	17,521,119
Other comprehensive income (expense):		
Gain (loss) on foreign currency translation	(773)	1,595
Unrealized gain (loss) on short-term investments	15	(46)
Total comprehensive loss	$(62,274)	$(28,248)

The accompanying notes are an integral part of these consolidated financial statements.

Savara Inc. and Subsidiaries

Consolidated Statements of Changes in Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)

Year Ended December 31, 2018

(in thousands, except share amounts)

	Redeemable Convertible Preferred Stock							Stockholders' Equity (Deficit)			
	Redeemable Convertible Series A Preferred Stock		Redeemable Convertible Series B Preferred Stock		Redeemable Convertible Series C Preferred Stock			Common Stock		Additional Paid-In	Accumu
	Number of Shares	Amount	Number of Shares	Amount	Number of Shares	Amount	Total	Number of Shares	Amount	Capital	Deficit
, 2016	1,799,906	$3,232	5,675,387	$17,301	4,452,582	$23,328	$43,861	3,162,573	$5	$3,117	$(38,40
	—	—	—	—	—	—	—	(19,045)	—	—	—
ck	—	22	—	460	—	96	578	—	—	(578)	—
ck upon	—	—	—	—	—	—	—	111,799	—	384	—
e notes	—	—	—	—	—	—	—	1,140,046	1	10,044	—
le											
as											
Ratio	(1,799,906)	(3,254)	(5,675,387)	(17,761)	(4,452,582)	(23,424)	(44,439)	7,034,102	7	44,431	—
nt	—	—	—	—	—	—	—	—	—	370	—
ature	—	—	—	—	—	—	—	—	—	404	—
on	—	—	—	—	—	—	—	3,639,189	4	35,842	—
ck upon	—	—	—	—	—	—	—	15,071,710	15	89,583	—
arrants	—	—	—	—	—	—	—	—	—	359	—
ck upon	—	—	—	—	—	—	—	198,298	—	1,665	—

ck for	—	—	—	—	—	—	—	75,486	—	—	—
ck upon	—	—	—	—	—	—	—	92,446	—	—	—
ck upon	—	—	—	—	—	—	—	2,918	—	5	—
	—	—	—	—	—	—	—	—	—	344	—
on	—	—	—	—	—	—	—	—	—	552	—
ation	—	—	—	—	—	—	—	—	—	—	—
-term	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	(29,79
, 2017	—	$—	—	$—	—	$—	$—	30,509,522	$32	$186,522	$(68,20
ck upon	—	—	—	—	—	—	—	4,250,000	4	45,788	—
ck upon net	—	—	—	—	—	—	—	48,600	—	505	—
ck for	—	—	—	—	—	—	—	50,625	—	—	—
ck upon	—	—	—	—	—	—	—	115,754	—	—	—
ck upon	—	—	—	—	—	—	—	61,893	—	58	—
ck upon	—	—	—	—	—	—	—	2,123	—	19	—
r	—	—	—	—	—	—	—	107,579	—	995	—
arrants	—	—	—	—	—	—	—	—	—	78	—
on	—	—	—	—	—	—	—	—	—	3,737	—
ation	—	—	—	—	—	—	—	—	—	—	—
-term	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	(61,51
, 2018	—	$—	—	$—	—	$—	$—	35,146,096	$36	$237,702	$(129,7

The accompanying notes are an integral part of these consolidated financial statements.

Savara Inc. and Subsidiaries

Consolidated Statements of Cash Flows

(in thousands)

	Years ended December 31,	
	2018	2017
Cash flows from operating activities:		
Net loss	$(61,516)	$(29,797)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	526	363
Impairment of acquired IPR&D	21,692	—
Change in fair value of financial instruments	64	280
Change in fair value of contingent consideration	266	2,240
Non-cash interest	75	336
Loss on extinguishment of debt	—	1,816
Write-off of acquired IPR&D	995	—
Foreign currency (gain) loss	(71)	218
Amortization of debt issuance costs	468	401
Accretion on discount to short-term investments and convertible promissory notes	(900)	(136)
Stock-based compensation	3,737	552
Issuance of call option derivative	—	344
Benefit for deferred taxes	(7,057)	(2,820)
Changes in operating assets and liabilities:		
Grant and award receivable	—	400
Prepaid expenses and other current assets	900	(2,564)
Accounts payable and accrued expenses and other current liabilities	1,546	133
Net cash used in operating activities	$(39,275)	$(28,234)
Cash flows from investing activities:		
Cash acquired through Merger	$—	$3,442
Purchase of property and equipment	(141)	(495)
Purchase of available-for-sale securities, net	(122,494)	(76,862)
Maturities of available-for-sale securities	98,746	4,800
Sales of available-for-sale securities, net	10,270	—
Net cash used in investing activities	$(13,619)	$(69,115)
Cash flows from financing activities:		
Proceeds from debt facility, net	$9,365	$11,327
Issuance of common stock upon exercise of warrants	19	384
Issuance of common stock upon public offering, net	45,792	89,598
Issuance of common stock upon at the market offerings, net	505	1,666
Proceeds from exercise of stock options	58	5
Proceeds from convertible promissory notes, net	—	3,569
Capital lease obligation principal payments	(546)	(460)
Net cash provided by financing activities	$55,193	$106,089
Effect of exchange rate changes on cash and cash equivalents	(119)	8
Increase in cash and cash equivalents	$2,180	$8,748
Cash and cash equivalents beginning of period	22,121	13,373

Cash and cash equivalents end of period	$24,301	$22,121
Non-cash transactions:		
Extinguishment and derecognition of put options	$—	$2,202
Conversion of convertible notes into common stock	—	8,249
Shares issued in connection of business combination and assumed equity awards	—	35,846
Accretion of redeemable convertible preferred stock	—	578
Beneficial conversion feature	—	404
Common stock issued for IPR&D, net	995	—
Supplemental disclosure of cash flow information:		
Cash paid for interest	$1,406	$733

The accompanying notes are an integral part of these consolidated financial statements.

Savara Inc. and Subsidiaries

Notes to Consolidated Financial Statements

1. Description of Business and Basis of Presentation

Description of Business

Savara Inc. ("Savara," the "Company," or as used in the context of "we" or "us") is an orphan lung disease company. The Company's pipeline comprises Molgradex, an inhaled granulocyte-macrophage colony-stimulating factor ("GM-CSF") in Phase 3 development for autoimmune pulmonary alveolar proteinosis ("aPAP"), in Phase 2a development for nontuberculous mycobacterial ("NTM") lung infection, and in preparation for Phase 2a development in cystic fibrosis ("CF") affected individuals with chronic NTM lung infection, and AeroVanc, a Phase 3 stage inhaled vancomycin for treatment of persistent methicillin-resistant Staphylococcus aureus ("MRSA") lung infection in individuals living with CF. The Company and its wholly-owned subsidiaries operate in one segment with its principal offices in Austin, Texas.

On April 27, 2017, Savara completed its business combination with Mast Therapeutics, Inc. ("Mast"), a publicly held company, in accordance with the terms of the Agreement and Plan of Merger and Reorganization (the "Merger Agreement"), dated January 6, 2017 (the "Merger"). In connection with and immediately prior to the effective time of the Merger, Mast implemented a reverse stock split at a ratio of one new share for every 70 shares of its common stock outstanding (the "Reverse Stock Split"). Under the terms of the Merger Agreement, each outstanding share of Savara common stock was then converted into Mast common stock at a ratio of approximately .5860 of a Savara share (the "Exchange Ratio"). Immediately following the effective date of the Merger, Mast's pre-existing equity holders owned approximately 23% of the combined company, and Savara's pre-existing equity holders owned approximately 77%. Accordingly, all operations presented in the accompanying financial statements and notes to the financial statements represent the historical activity of Savara, the private company prior to and accounting acquirer in the Merger.

The accompanying consolidated financial statements and notes to the consolidated financial statements also give retroactive effect to the common stock Exchange Ratio and Reverse Stock Split for all periods presented, including common stock warrants and common stock-based compensation awards.

Following the Merger, Mast was renamed "Savara Inc." and its common stock is trading on The Nasdaq Global Select Market under the symbol "SVRA." Prior to the Merger, Mast's common stock was traded on the New York Stock Exchange under the symbol "MSTX."

Since inception, Savara has devoted substantially all of its efforts and resources to identifying and developing its product candidates, recruiting personnel, and raising capital. Savara has incurred operating losses and negative cash flow from operations and has no product revenue from inception to date. The Company has not yet commenced commercial operations.

Basis of Presentation

The consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States ("U.S. GAAP") as defined by the Financial Accounting Standards Board (the "FASB"). Certain prior year amounts have been reclassified for consistency with the current period presentation.

2. Summary of Significant Accounting Policies

Liquidity

As of December 31, 2018, the Company had an accumulated deficit of approximately $129.7 million. The Company used cash from operations of approximately $39.3 million for the year ended December 31, 2018. The cost to further develop and obtain regulatory approval for any drug is substantial and, as noted below, the Company may have to take certain steps to maintain a positive cash position. Accordingly, the Company will need additional capital to further fund the development of, and seek regulatory approvals for, its product candidates and begin to commercialize any approved products.

Currently, the Company is primarily focused on the development of respiratory drugs and believes such activities will result in the Company's continued incurrence of significant research and development and other expenses related to those programs. If the clinical trials for any of the Company's product candidates fail or produce unsuccessful results and those product candidates do not gain regulatory approval, or if any of the Company's product candidates, if approved, fail to achieve market acceptance, the Company may never become profitable. Even if the Company achieves profitability in the future, it may not be able to sustain profitability in subsequent periods. The Company intends to cover its future operating expenses through cash and cash equivalents on hand and through a combination of equity offerings, debt financings, government or other third-party funding, and other collaborations and strategic alliances. The Company cannot be sure that additional financing will be available when needed or that, if available, financing will be obtained on terms favorable to the Company or its stockholders.

The Company had cash and cash equivalents of $24.3 million and short-term investments of $86.5 million as of December 31, 2018, which is sufficient to fund the Company's operations for the twelve months subsequent to the issuance date of its consolidated financial statements for the year ended December 31, 2018. We intend to continue to raise additional capital as needed through the issuance of additional equity and potentially through borrowings, and strategic alliances with partner companies. However, if such financings are not available timely and at adequate levels, the Company will need to re-evaluate its long-term operating plans. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Principles of Consolidation

The consolidated financial statements of the Company are stated in U.S. dollars. These financial statements include the accounts of the Company and its wholly-owned subsidiaries. The financial statements of the Company's wholly-owned subsidiaries are recorded in their functional currency and translated into the reporting currency. The cumulative effect of changes in exchange rates between the foreign entity's functional currency and the reporting currency is reported in "Accumulated other comprehensive income." All intercompany transactions and accounts have been eliminated in consolidation.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires the Company to make certain estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Management's estimates include those related to the accrual of research and development costs, the valuation of preferred and common shares, certain financial instruments recorded at fair value, stock-based compensation, contingent consideration, and the valuation allowance for deferred tax assets. The Company bases its estimates on historical experience and on various other market-specific and relevant assumptions that it believes to be reasonable under the circumstances. Accordingly, actual results could be materially different from those estimates.

Risks and Uncertainties

The product candidates being developed by the Company require approval from the U.S. Food and Drug Administration (the "FDA") or foreign regulatory agencies prior to commercial sales. There can be no assurance that the Company's product candidates will receive the necessary approvals. If the Company is denied regulatory approval of its product candidates, or if approval is delayed, it may have a material adverse impact on the Company's business, results of operations and financial position.

The Company is subject to a number of risks similar to other life science companies, including, but not limited to, risks related to the successful discovery and development of drug candidates, raising additional capital, development of competing drugs and therapies, protection of proprietary technology and market acceptance of the Company's products. As a result of these and other factors and the related uncertainties, there can be no assurance of the Company's future success.

Cash and Cash Equivalents

Cash and cash equivalents consist of cash and institutional bank money market accounts with original maturities of three months or less when acquired and are stated at cost, which approximates fair value.

Short-term Investments

The Company has classified its investments in debt securities with readily determinable fair value as available-for-sale securities. These securities are carried at estimated fair value with the aggregate unrealized gains and losses related to these investments, net of taxes, reflected as a part of "Accumulated other comprehensive income" within stockholders'

equity.

The fair value of the investments is based on the specific quoted market price of the securities or comparable securities at the balance sheet date. Investments in debt securities are considered to be impaired when a decline in fair value is judged to be other than temporary because the Company either intends to sell or it is more-likely-than not that it will have to sell the impaired security before recovery. Once a decline in fair value is determined to be other than temporary, an impairment charge is recorded and a new cost basis in the investment is established.

Concentration of Credit Risk

Financial instruments, which potentially subject the Company to concentrations of credit risk, consist principally of cash and cash equivalents and foreign exchange derivatives not designated as hedging. The Company places its cash and cash equivalents with a limited number of financial institutions and at times may exceed the amount of insurance provided on such deposits.

Accrued Research and Development Costs

The Company records the costs associated with research, nonclinical studies, clinical trials, and manufacturing development as incurred. These costs are a significant component of the Company's research and development expenses, with a substantial portion of the Company's on-going research and development activities conducted by third-party service providers, including contract research and manufacturing organizations.

The Company accrues for expenses resulting from obligations under agreements with contract research organizations ("CROs"), contract manufacturing organizations ("CMOs"), and other outside service providers for which payment flows do not match the periods over which materials or services are provided to the Company. Accruals are recorded based on estimates of services received and efforts expended pursuant to agreements established with CROs, CMOs, and other outside service providers. These estimates are typically based on contracted amounts applied to the proportion of work performed and determined through analysis with internal personnel and external service providers as to the progress or stage of completion of the services. The Company makes significant judgments and estimates in determining the accrual balance in each reporting period. In the event advance payments are made to a CRO, CMO, or outside service provider, the payments will be recorded as a prepaid asset that will be amortized as the contracted services are performed. As actual costs become known, the Company adjusts its prepaids and accruals. Inputs, such as the services performed, the number of patients enrolled, or the study duration, may vary from the Company's estimates resulting in adjustments to research and development expense in future periods. Changes in these estimates that result in material changes to the Company's accruals could materially affect the Company's results of operations. The Company has not experienced any material deviations between accrued and actual research and development expenses.

Business Combinations

Assets acquired and liabilities assumed as part of a business acquisition are recorded at their estimated fair value at the date of acquisition. The excess of purchase price over the fair value of assets acquired and liabilities assumed is recorded as goodwill. Determining fair value of identifiable assets, particularly intangibles, and liabilities acquired also requires management to make estimates, which are based on all available information and, in some cases, assumptions with respect to the timing and amount of future revenue and expenses associated with an asset.

Goodwill, Acquired In-Process Research and Development and Deferred Tax Liability

Goodwill represents the excess of purchase price over the fair value of net assets acquired by the Company. Goodwill is not amortized, but assessed for impairment on an annual basis or more frequently if impairment indicators exist. Recent guidance issued by the FASB, as previously adopted by the Company, provides an impairment model whereby the Company has the option to implement a one-step method for determining impairment of goodwill, simplifying the subsequent measurement of goodwill by eliminating Step 2 (measuring a goodwill impairment loss by comparing the implied fair value of a reporting unit's goodwill with the carrying amount of that goodwill) from the goodwill impairment test. Under the amendments in this guidance, an entity should perform its annual, or interim, goodwill impairment test by comparing the fair value of a reporting unit with its carrying amount. An entity should recognize an impairment charge for the amount by which the carrying amount exceeds the reporting unit's fair value; however, the loss recognized should not exceed the total amount of goodwill allocated to that reporting unit. Additionally, an entity should consider income tax effects from any tax deductible goodwill on the carrying amount of the reporting unit when measuring the goodwill impairment loss, if applicable.

Acquired in-process research and development ("IPR&D") is considered an indefinite-lived intangible asset and is assessed for impairment annually or more frequently if impairment indicators exist. The Company adopted accounting guidance related to annual and interim acquired IPR&D impairment test, a two-step method, which allows the Company to first assess qualitative factors before performing a quantitative assessment of the fair value of a reporting unit. If it is determined on the basis of qualitative factors that the fair value of the reporting unit is more likely than not

less than the carrying amount, a quantitative impairment test is required.

If the associated research and development effort is abandoned, the related asset will be written-off, and the Company will record a noncash impairment loss on its consolidated statements of operations and comprehensive loss. For those products that reach commercialization, the IPR&D asset will be amortized over its estimated useful live.

The Company performs its annual goodwill impairment test and IPR&D impairment test, as described above, as of June 30th and September 30th, respectively, or whenever an event or change in circumstances occurs that would require reassessment of the recoverability of those assets. During the year ended December 31, 2018, the Company experienced a $0.2 million and $0.6 million decrease in the carrying value of goodwill and IPR&D, respectively, related to its acquisition of Serendex A/S ("Serendex") on July 15, 2016, which was due to foreign currency translation. In addition, during the year ended December 31, 2018, the Company recorded $21.7 million of impairment charges and a corresponding decrease to the carrying value of IPR&D related to the Aironite drug candidate assumed in the Merger (as defined and further described in Note 7) due to the unfavorable results from a Phase 2 study that demonstrated a failure of Aironite to meet the endpoints of the study and limited effectiveness of the compound in patients. As a result of the IPR&D impairment charges recorded in the first quarter of 2018, the Company reduced the associated deferred tax liability related to the acquired IPR&D from the Merger by $4.6 million and recorded an income tax benefit. The Company additionally performed impairment tests for goodwill and IPR&D as of June 30, 2018 and September 30, 2018, respectively, and noted there have been no further triggering events or indicators of impairment as of December 31, 2018.

Tax Refund Receivable

The Company has recorded a Danish tax credit earned by its subsidiary, Savara ApS, for the year ended December 31, 2018. Under Danish tax law, Denmark remits a research and development tax credit equal to 22% of qualified research and development expenditures, not to exceed established thresholds. As of December 31, 2018, credits totaling $0.8 million had been generated but not yet received and are recorded in "Prepaid expenses and other current assets" and expected to be received in the fourth quarter of 2019.

The Company also recognized an income tax benefit for the year ended December 31, 2018 as provided by the Australian Taxation Office for qualified research and development expenditures on the NTM program incurred through our subsidiary, Savara Australia Pty. Limited. Under Australian tax law, Australia remits a research and development tax credit equal to 43.5% of qualified research and development expenditures, not to exceed established thresholds. As of December 31, 2018, credits totaling $0.5 million had been generated but not yet received and are recorded in "Prepaid expenses and other current assets" and expected to be received in the fourth quarter of 2019.

Segment Reporting

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, or decision making group, in making decisions on how to allocate resources and assess performance. Our chief operating decision maker is the chief executive officer. We have one operating segment, specialty pharmaceuticals within the respiratory system.

Fair Value of Financial Instruments

The accounting standard for fair value measurements provides a framework for measuring fair value and requires disclosures regarding fair value measurements. Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date, based on the Company's principal market or, in absence of a principal market, most advantageous market for the specific asset or liability.

The Company uses a three-tier fair value hierarchy to classify and disclose all assets and liabilities measured at fair value on a recurring basis, as well as assets and liabilities measured at fair value on a non-recurring basis, in periods subsequent to their initial measurement. The hierarchy requires the Company to use observable inputs when available, and to minimize the use of unobservable inputs, when determining fair value.

The three tiers are defined as follows:

- Level 1 – Observable inputs that reflect quoted market prices (unadjusted) for identical assets or liabilities in active markets;
- Level 2 – Observable inputs other than quoted prices in active markets that are observable either directly or indirectly in the marketplace for identical or similar assets and liabilities; and
- Level 3 – Unobservable inputs that are supported by little or no market data, which require the Company to develop its own assumptions.

Financial instruments carried at fair value include: (i) cash and cash equivalents, (ii) short-term investments, (iii) contingent consideration related to the acquisition of Serendex on July 15, 2016 for which any change is reflected in general and administrative expense, and (iv) foreign exchange derivatives.

Financial instruments not carried at fair value include accounts payable and accrued liabilities. The carrying amounts of these financial instruments approximate fair value due to the highly liquid nature of these short-term instruments.

Property and Equipment

Property and equipment are stated at cost, net of accumulated depreciation. Depreciation is determined on a straight-line basis over the estimated useful lives of the assets, which range from three to five years. Repairs and maintenance that do not improve or extend the useful life of the respective asset are charged to expense as incurred.

Equipment under Capital Lease

In 2015, the Company entered into a contract manufacturing arrangement that included the right to use specified equipment. Management concluded that the contract manufacturing arrangement contains an embedded lease of the specified equipment based on the facts and circumstances, including the Company's ability to direct the use of the equipment and because management believes that it is remote that any party other than the Company will take more than a minor output produced by the equipment during the term of the arrangement. Management performed an analysis under Accounting Standards Codification ("ASC") 840, "Leases" to determine the proper accounting for the embedded lease and concluded that there is a capital lease because the present value of the minimum lease payments per the contract exceeds 90% of the fair value of the equipment. The capitalized equipment is depreciated on a straight-line basis over the lesser of the non-cancellable lease term or the useful life, and the lease obligation accrues interest at the incremental rate used in the present value analysis.

Patents and Intellectual Property

As the Company's products are currently under research and development and are not currently approved for market, costs incurred in connection with patent applications are expensed as incurred due to the uncertainty of the future economic benefits of the underlying patents and intellectual property.

Revenue Recognition

The Company will record revenue based on a five-step model in accordance with ASC 606, "Revenue from Contracts with Customers." To date, the Company has not generated any product revenue from its drug candidates. The Company's ability to generate product revenues, which the Company does not expect will occur in the next two to three years, if ever, will depend heavily on the successful development, regulatory approval and eventual commercialization of the Company's product candidates.

Milestone Revenue

The Company is subject to various license agreements related to its product candidates, as discussed further under Note 16, which includes certain milestone payments to be remunerated by the licensee to Savara. Pursuant to the license agreement, the Company identifies the performance obligations, determines the transaction price, allocates the contract transaction price to the performance obligations, and recognizes the revenue when (or as) the performance obligation is satisfied. The Company identifies the performance obligations included within the license agreement and evaluates which performance obligations are distinct.

The milestone payments are a form of variable consideration as the payments are contingent upon achievement of a substantive event. The milestone payments are estimated and included in the transaction price when the Company determines, under the variable consideration constraint, that it is probable that there will not be a significant reversal of cumulative revenue recognized in future periods. The transaction price is then allocated to each performance

obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such milestones and any related constraint, and if necessary, adjusts the estimate of the overall transaction price.

Net Loss per Share

Basic net loss attributable to common stockholders per share is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock, pre-funded warrants, restricted stock and restricted stock units outstanding during the period without consideration of common stock equivalents. Since the Company was in a loss position for all periods presented, diluted net loss per share is the same as basic net loss per share for all periods presented as the inclusion of all potential dilutive securities would have been antidilutive.

Redeemable Convertible Preferred Stock and Series B and Series C Warrants

In connection with the Merger, the Series A, Series B, and Series C redeemable convertible preferred stock, previously classified in temporary equity as it was redeemable at the written request of the holders of at least two-thirds of the then-outstanding shares of preferred stock, at any time after October 31, 2022, was converted to common stock subject to the Exchange Ratio. Additionally, certain outstanding warrants to purchase Series B convertible preferred stock ("Series B Warrants") previously classified as liabilities were exercised on the effective date of the Merger or subsequently expired in May 2017. Certain outstanding warrants to purchase Series C redeemable convertible preferred stock ("Series C Warrants") were reclassified from a liability to common equity as they were converted to warrants to purchase common stock subject to the Exchange Ratio following the Merger.

Stock-Based Compensation

The Company recognizes the cost of stock-based awards granted to employees based on the estimated grant-date fair value of the awards. The value of the portion of the award that is ultimately expected to vest is recognized as expense ratably over the requisite service period. The Company recognizes the compensation costs for awards that vest over several years on a straight-line basis over the vesting period (see Note 15). Forfeitures are recognized when they occur, which may result in the reversal of compensation costs in subsequent periods as the forfeitures arise. The Company recognizes the cost of stock-based awards granted to non-employees at their then-current fair values as services are performed and such awards are remeasured through the counterparty performance date.

Manufacturing and Other Commitments and Contingencies

The Company is subject to various manufacturing royalties and payments related to its product candidate, Molgradex. Under an agreement, as amended, with the Active Pharmaceutical Ingredients ("API") manufacturer, no signing fee or milestones are included in the royalty payments, and there is no minimum royalty. Upon the successful development, registration and attainment of approval by the proper health authorities, such as the FDA, in any territory except Latin America, Central America and Mexico, the Company must pay a royalty of three percent (3%) on annual net sales to the manufacturer of its API. Additionally, Savara must make certain payments to the API manufacturer upon achievement of the milestones outlined in the table set forth below.

Pursuant to a license agreement (Note 16) between the Company and a Japanese licensee regarding the development and commercialization of Molgradex for the treatment of aPAP in Japan, the Company shall fund the licensee fifty percent (50%), up to a maximum of approximately $0.8 million, of the external costs associated with specific research, regulatory and filing activities to be conducted by the licensee.

Under an agreement with a medical education and research foundation entered into on October 8, 2018, the Company is subject to a milestone payment for the use of proprietary information and material in intellectual property filings related to the application of Molgradex in the treatment of NTM. The Company will owe royalties to the foundation based on net sales of Molgradex for the treatment of NTM equal to one half of one percent (0.5%) after publication of the intellectual property filings and one quarter of one percent (0.25%) prior to the publication or in the event publication does not occur, with respect to the specified intellectual property filings.

The Company is also subject to certain contingent milestone payments, disclosed in the following table, payable to the manufacturer of the nebulizer used to administer Molgradex. In addition to these milestones, the Company will owe a royalty to the manufacturer of the nebulizer based on net sales. The royalty rate ranges from three and one half percent (3.5%) to five percent (5%) depending on the device technology used by the Company to administer the product.

Manufacturing and Other Contingent Milestone and Co-Development Payments (in thousands):

	December 31, 2018
Molgradex API manufacturer:	
Achievement of certain regulatory milestones for the approval of Molgradex and the delivery of working and master cell banks	$ 2,600
Molgradex nebulizer manufacturer:	
Achievement of various development activities and regulatory approval of nebulizer utilized to administer Molgradex	7,962
Molgradex Japanese licensee:	
Co-development and regulatory costs	750
Medical education and research foundation:	
First commercial sale in the U.S. of Molgradex in treatment of NTM	500
Total manufacturing and other commitments	$ 11,812

As of December 31, 2018 and 2017, none of the above milestones or co-development commitments had been met or incurred.

Income Taxes

The Company uses the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the carrying amounts and the tax basis of assets and liabilities. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect of a change in tax rates on deferred tax assets and liabilities will be recognized in the period that includes the enactment date. A valuation allowance is established against the deferred tax assets to reduce their carrying value to an amount that is more-likely-than not to be realized.

Recent Accounting Pronouncements

In May 2014, the FASB issued Accounting Standards Update (“ASU”) 2014-09, “Revenue from Contracts with Customers” and has subsequently issued several supplemental and/or clarifying ASUs, which comprise the new comprehensive revenue recognition standard that replaces all current U.S. GAAP guidance on this topic and eliminate all industry-specific guidance. The standard’s core principle is that a reporting entity will recognize revenue when it transfers promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The Company has adopted this standard and its impact on its consolidated financial statements and related disclosures is immaterial.

In February 2016, the FASB issued ASU 2016-02, “Leases.” The update aims to make leasing activities more transparent and comparable and requires substantially all leases be recognized by lessees on their balance sheet as a right-of-use asset and a corresponding lease liability, including leases currently accounted for as operating leases. The update also requires improved disclosures to help users of financial statements better understand the amount, timing and uncertainty of cash flows arising from leases. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018 with early adoption permitted. The Company has assessed and determined that the impact of the adoption of ASU 2016-02 will be immaterial on its consolidated financial statements and disclosures, and expects the impact to be limited to the operating lease agreements for the office spaces in Austin, Texas; Copenhagen, Denmark; and San Diego, California which is currently being subleased.

In January 2017, the FASB issued ASU 2017-01, “Business Combinations (Topic 805): Clarifying the Definition of a Business,” which intends 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. ASU 2017-01 is effective for fiscal years beginning after December 15, 2017 with early adoption permitted. The Company has adopted this standard and the impact on its consolidated financial statements and related disclosures is immaterial.

In June 2018, the FASB issued ASU 2018-07, “Stock Compensation (Topic 718): Improvements to Non-employee Share-Based Payment Accounting.” The update aims to simplify the accounting for share-based payments to non-employees by aligning it with the accounting for share-based payments to employees. The standard is effective for fiscal years beginning after December 15, 2018 with early adoption permitted. The Company does not expect the adoption of ASU 2018-07 to have a material impact on its consolidated financial statements.

3. Prepaid expenses and other current assets

Prepaid expenses, consisted of (in thousands):

	December 31,	
	2018	2017
R&D tax credit receivable	$1,263	$834
Prepaid clinical trial costs	561	2,129
VAT receivable	421	196
Prepaid insurance	162	158
Forward currency exchange derivative	—	40
Deposits and other	107	194
Total prepaid expenses and other current assets	$2,514	$3,551

4. Accrued expenses and other current liabilities

Accrued expenses and other liabilities, consisted of (in thousands):

	December 31,	
	2018	2017
Accrued contracted research and development costs	$2,044	$1,308
Accrued general and administrative costs	371	323
Accrued compensation	643	1,328
Forward currency exchange derivative	26	—
Deferred revenue	250	—
Other	—	7
Total accrued expenses and other current liabilities	$3,334	$2,966

5. Short-term Investments

Short-term Investments in Available-for-Sale Securities

The Company’s investment policy seeks to preserve capital and maintain sufficient liquidity to meet operational and other needs of the business. The following table summarizes, by major security type, the Company’s investments (in thousands):

As of December 31, 2018	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Short-term investments				
U.S. government securities	$ 15,967	$ —	$ (2)	$15,965
Asset backed securities	8,595	—	(7)	8,588
Corporate securities	19,975	—	(21)	19,954

Commercial paper	42,022	—	—	42,022
Total short-term investments	$ 86,559	$ —	$ (30)	$ 86,529

As of December 31, 2017	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Short-term investments				
U.S. government securities	$ 11,894	$ —	$ (9)	$ 11,885
Asset backed securities	8,389	—	(6)	8,383
Corporate securities	22,113	—	(31)	22,082
Commercial paper	29,842	—	—	29,842
Total short-term investments	$ 72,238	$ —	$ (46)	$ 72,192

The Company has classified its investments as available-for-sale securities. These securities are carried at estimated fair value with the aggregate unrealized gains and losses related to these investments reflected as a part of "Accumulated other comprehensive income" in the consolidated balance sheets. Classification as short-term or long-term is based upon whether the maturity of the debt securities is less than or greater than twelve months.

There were no significant realized gains or losses related to investments for the years ended December 31, 2018 and 2017.

6. Property and Equipment, Net

Property and equipment, net consisted of (in thousands):

	December 31,	
	2018	2017
Research and development equipment under capital lease	$1,102	$1,102
Equipment	625	674
Furniture and fixtures	163	—
Total property and equipment	1,890	1,776
Less accumulated depreciation	(1,368)	(851)
Property and equipment, net	$522	$925

Depreciation expense for the years ended December 31, 2018 and 2017 was $0.5 million and $0.4 million, respectively, and includes the amortization of the capital lease.

7. Acquisitions

Mast

On April 27, 2017, the Company completed the Merger with Mast as discussed in Note 1. The Merger was accounted for as a reverse merger under the acquisition method of accounting whereby Savara was considered to have acquired Mast for financial reporting purposes because, immediately upon completion of the Merger, Savara stockholders held a majority of the voting interest of the combined company.

Pursuant to business combination accounting, the Company applied the acquisition method, which requires the assets acquired and liabilities assumed be recorded at fair value with limited exceptions. The Company used the Multi-Period Excess Earnings Model, MPEEM, a form of the income approach to value the in-process research and development intangible asset. Under the valuation method, the present value of future cash flows expected to be generated from the in-process research and development of the acquired product candidate, Aironite, was determined using a reasonable discount rate, and identified projected cash flows from Aironite were risk adjusted to take into consideration the probabilities of moving through the various clinical stages. The excess of the purchase price over the assets acquired and liabilities assumed represents goodwill. The goodwill is primarily attributable to the synergies expected to arise after the acquisition and is not expected to be deductible for tax purposes. Transaction costs associated with the Merger of approximately $2.2 million are included in general and administrative expense for the year ended December 31, 2017. The total purchase price for Mast was $35.8 million based on the fair value of the outstanding Mast equity on the date of the Merger, which was allocated as follows:

Purchase Consideration	(in thousands)
Fair value of Mast shares outstanding	$ 33,117
Fair value of Mast equity	2,729
Fair value of total consideration	$ 35,846
Assets acquired and liabilities assumed	
Cash and cash equivalents	$ 3,442
Tangible assets	283
In-process research and development intangible assets	21,692
Liabilities	(2,396)
Debt	(3,407)
Deferred tax liability	(7,375)
Total assets acquired and liabilities assumed	12,239
Goodwill	23,607
Total	$ 35,846

During the year ended December 31, 2018, the Company finalized the purchase price allocation which did not result in any adjustments to the previous allocation.

As discussed in Note 2, during the first quarter of 2018, the Company recorded a $21.7 million impairment charge and corresponding decrease to the carrying value of IPR&D recorded with respect to the Merger to write the IPR&D asset off in full due to the failure of Aironite to meet its primary and secondary endpoints in the Phase 2 study. Following the negative outcome of the study, Savara does not plan to support any new development of Aironite. The decrease in the carrying value of IPR&D has been recognized as an expense to “Impairment of acquired IPR&D” included in the consolidated statement of operations and comprehensive loss for the year ended December 31, 2018. As a result of the impairment charge recorded in the first quarter of 2018, the Company reduced the related deferred tax liability by $4.6 million and recorded an income tax benefit.

Mast Pro Forma (Unaudited)

The following summary pro forma financial information reflects the consolidated operations of the Company for the year ended December 31, 2017 as if the Merger with Mast had occurred on January 1, 2016. This summary pro forma information is not necessarily representative of what the Company’s results of operations would have been had the Merger in fact occurred on January 1, 2016, and is not intended to project the Company’s results of operations for any future period. Included in the Savara consolidated statement of operations for the year ended December 31, 2017 is $0 of revenue and $1.6 million of net loss before income tax generated by Mast since April 27, 2017, the acquisition date.

	Year ended December 31, 2017
Net revenues	$ 94
Net loss	$ (20,420)

Cardeas

In June 2018, the Company entered into an asset purchase agreement (the “Purchase Agreement”) with Cardeas Pharma Corporation (“Cardeas”), a biopharmaceutical company specializing in the development of inhaled antibiotics to treat hospital-acquired and/or multi-drug resistant bacterial respiratory infections from highly antibiotic-resistant organisms. Pursuant to the Purchase Agreement, Savara acquired substantially all of the assets, including intellectual property, of Cardeas for a purchase price comprised of (i) an upfront payment of 107,579 shares of the Company’s common stock equal to approximately $1.0 million as of the date of consummation which was recorded to “Research and development” expense included in the consolidated statement of operations and comprehensive loss for the year ended December 31, 2018 and (ii) certain contingent payments due upon the achievement of distinct development milestones. The Company accounted for the transaction as an asset purchase. As of the measurement date of the acquisition and at December 31, 2018, the Company deemed the contingent payments are not probable and, as such, has not recorded an associated liability but will continue to assess at each period accordingly.

8. Convertible Promissory Notes

A. 2016 Convertible Promissory Note

During 2016, the Company borrowed approximately $4.4 million from several investors under convertible subordinate promissory notes, which were subsequently amended (the “2016 Notes”). Under the amended terms, the 2016 Notes converted into equity in connection with the Merger.

The 2016 Notes accrued interest at 8.0% per annum computed on the basis of the actual number of days elapsed and a 365-day year. All unpaid principal, together with any then accrued but unpaid interest was due and payable on the earliest of (i) June 30, 2018 (the “Maturity Date”), (ii) the closing of a change of control as defined in the 2016 Notes, or (iii) the occurrence of an event of default, as defined in the 2016 Notes (such earliest date is hereinafter referred to as maturity). The 2016 Notes were prepayable only with the written consent of the holders of a majority of the principal amount of the then-outstanding 2016 Notes. The 2016 Notes were convertible into the Company’s equity upon the occurrence of the following events: (i) a qualified private financing, (ii) a non-qualified private financing or the consummation of a qualified or non-qualified Regulation A public offering, (iii) a change of control, (iv) upon an initial public offering of the Company’s common stock, (v) the Maturity Date, and (vi) a public listing of the Company further described below.

The 2016 Notes and the Series C Warrants, issued with the note subscriptions, were amended to convert if shares of the Company's capital stock became listed on a national exchange or were exchanged for such listed shares (a "Public Listing Conversion"). The amendment provides the warrant holder the right to voluntarily exercise the Series C Warrants for common shares following the Merger, and the 2016 Notes would be automatically converted in the case of the Merger. Upon the consummation of the Merger or a similar Public Listing Conversion, the entire principal amount plus any accrued interest under the 2016 Notes automatically converts into shares of common stock at $4.22 per share, which was 80% of the estimated Merger per share value, for notes issued on or prior to August 15, 2016 and 80% of the average trading price of Mast's common stock for the twenty day period ending two days prior to the closing of the Merger, as adjusted by the Exchange Ratio described in the Merger Agreement.

Accounting for the 2016 Notes

Upon the issuance of the 2016 Notes, management determined that the automatic conversion features upon a qualified private financing, a qualified Regulation A public offering, a non-qualified private financing, and a non-qualified Regulation A public offering discussed above represented, in substance, a put option (redemption feature) designed to provide the investor with a fixed monetary amount, settleable in shares. Management determined that this put option should be separated and accounted for as a derivative primarily because the put option met the net settlement criterion and the settlement provisions were not consistent with a fixed-for-fixed equity instrument. With respect to the Series C Warrants issued to investors who purchased 2016 Notes prior to August 15, 2016, management determined that the Series C Warrants should also be separated and accounted for as a derivative and classified as a liability.

Both the put option, with a fair value of approximately $1.0 million, and warrant liability, with a fair value of approximately $0.3 million, at inception, were initially recorded as derivative liabilities on the accompanying balance sheet and a corresponding discount to the 2016 Notes. The Company accreted the discount to interest expense on the statement of operations and comprehensive loss over the term of the 2016 Notes using the effective interest rate method. The Company recorded interest expense of $0.2 million during the year ended December 31, 2017 related to the accretion of the total discount through the date of conversion.

Upon the Merger, the date of the automatic conversion under the Public Listing Conversion provisions, the 2016 Notes were surrendered in exchange for shares of the Company's common stock after giving effect to the Exchange Ratio. The debt host contract and separated derivative liability were both subject to extinguishment accounting, and a loss in the amount of $0.9 million was recorded in the statement of operations and comprehensive loss for the year ended December 31, 2017. The loss was calculated as the difference between the net book value of the 2016 Notes plus the fair value of the put option immediately prior to the automatic conversion, and the fair value of the common stock into which the 2016 Notes were converted.

B. 2017 Convertible Promissory Notes

During 2017, the Company borrowed approximately $3.6 million from several investors under convertible subordinate promissory notes (the "2017 Notes"), which converted into equity in connection with the Merger. The 2017 Notes accrued interest at 8.0% per annum computed on the basis of the actual number of days elapsed and a 365-day year. All unpaid principal, together with any then accrued but unpaid interest was due and payable on the earliest of (i) June 30, 2018, (ii) the closing of a change of control as defined in the 2017 Notes, (iii) the occurrence of an event of default, as defined in the 2017 Notes, or (iv) a Public Listing Conversion (such earliest date is hereinafter referred to as maturity). The 2017 Notes were prepayable only with the written consent of the holders of a majority of the principal amount of the then-outstanding 2017 Notes. The terms and conditions of the 2017 Notes were substantially consistent with the 2016 Notes as described above, other than the terms for the conversion upon the event of a Public Listing Conversion which is described in regards to the 2017 Notes as follows:

Immediately prior to, but in any event conditioned upon, the consummation of a Public Listing Conversion, including the transactions described in the Merger Agreement, the entire outstanding principal amount of the 2017 Notes, any

accrued but unpaid interest and any other amounts payable under the 2017 Notes converts automatically into shares of the Company's common stock, as adjusted for the Exchange Ratio, at the Reverse Merger Conversion Price. Upon such occurrence, the 2017 Notes shall be converted into that number of shares of common stock determined by dividing (i) the aggregate outstanding principal amount of the 2017 Notes, any accrued but unpaid interest, and any other amounts payable under the 2017 Notes by (ii) the Reverse Merger Conversion Price which was eighty percent (80%) of the average trading price of Mast's common stock for the twenty-day period prior to the Merger.

Accounting for the 2017 Notes

Upon the issuance of the 2017 Notes, management determined that the automatic conversion upon a qualified private financing, a qualified Regulation A public offering, a non-qualified private financing, a non-qualified Regulation A public offering, and Public Listing Conversion feature as discussed above represented, in substance, a put option (redemption feature) designed to provide the investor with a fixed monetary amount, settleable in shares. Management determined that this put option should be separated and accounted for as a derivative primarily because the put option met the net settlement criterion and the settlement provisions were not consistent with a fixed-for-fixed equity instrument.

The put option, with a fair value of approximately $0.8 million at inception, was initially recorded as a derivative liability on the accompanying balance sheet and a corresponding discount to the 2017 Notes. The Company accreted the discount to interest expense on the statement of operations and comprehensive loss over the term of the 2017 Notes using the effective interest rate method. The Company recorded interest expense of approximately five thousand dollars during the year ended December 31, 2017 related to the accretion of the discount through the date of conversion.

Upon the Merger, the date of the automatic conversion under the Public Listing Conversion provisions, the 2017 Notes were surrendered in exchange for the Company's common stock after giving effect to the Exchange Ratio. The debt host contract and separated derivative liability were both subject to extinguishment accounting, and a loss in the amount of approximately $0.9 million was recorded in the statement of operations and comprehensive loss for the year ended December 31, 2017. The loss was calculated as the difference between the net book value of the 2017 Notes plus the fair value of the put option immediately prior to the automatic conversion, and the fair value of the common stock into which the 2017 Notes were converted.

9. Debt Facility

On April 28, 2017, the Company entered into a loan and security agreement with Silicon Valley Bank, as amended on October 31, 2017, (the "Loan Agreement"), which provided for a $15 million credit facility that was made available in two equal tranches. In December 2018, the Company entered into an amendment to the Loan Agreement (the "Amendment") to increase the amount of the term loan facility from $15 million to $45 million and make certain other changes. The Loan Agreement, as amended by the Amendment, provides that the funds are available in two tranches, (i) $25 million became available upon the effectiveness of the Amendment, of which $15 million was used to refinance the existing amount outstanding under the loan facility, and (ii) $20 million is to be made available upon the Company's request prior to September 30, 2019, subject to certain conditions. However, if the Company draws the second tranche, it will be required to provide cash collateral for $20 million if the Company's market cap falls below $200 million, until certain market cap requirements and thresholds are met.

Silicon Valley Bank has been granted a perfected first priority lien in all of our assets with a negative pledge on our intellectual property. The Loan Agreement contains customary affirmative and negative covenants, including among others, covenants limiting our ability and our subsidiaries' ability to dispose of assets, permit a change in control, merge or consolidate, make acquisitions, incur indebtedness, grant liens, make investments, make certain restricted payments and enter into transactions with affiliates, in each case subject to certain exceptions.

Following the Amendment, the loans bear interest at the prime rate reported in The Wall Street Journal, plus a spread of 3.0% (reduced from 4.25%). Interest only payments are due through October 2020 followed by monthly payments of principal plus interest over the following twenty-five (25) months and a maturity date of November 1, 2022. The Loan Agreement, as amended by the Amendment, includes (i) a prepayment fee (3.0% of funded amounts in months 1-12, 2.0% of funded amounts in months 13-24, and 1.0% thereafter); and (ii) an end of term charge equal to 6.0 % of the amount of principal borrowed. In connection with the Amendment, Savara paid Silicon Valley Bank a $0.6 million end of term payment fee. The prepayment penalty contemplated by the Loan Agreement was abated by Silicon Valley Bank. Additionally, Savara paid minimal legal costs directly attributable to the Amendment and previously paid $0.1 million in legal costs directly attributable to the original issuance of the debt instrument. 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.

The end of term charge equal to 6.0% of the amount of principal borrowed will be due on the scheduled maturity date and is being recognized as an increase to the principal with a corresponding charge to interest expense over the term of the facility using the effective interest method.

The Company evaluated the Loan Agreement, as amended by the Amendment, under ASC 470-50, “Debt - Modification and Extinguishment,” and concluded that the amended terms did not result in significant and consequential changes to the economic substance of the debt and thus resulted in a modification of the debt and not extinguishment of the debt.

Upon the funding of each tranche under the Loan Agreement (the first two $7.5 million tranches in 2017 and the $25.0 million tranche in connection with the Amendment), the Company was obligated to issue warrants to purchase shares of its common stock, as described below.

Upon funding the first tranche of the Loan Agreement, the Company was obligated to issue warrants to purchase shares of the Company’s common stock equal to 3.0% of the funded amount divided by the exercise price to be set based on the average price per share over the preceding 10 trading days prior to closing. As such, the Company issued a warrant for the first tranche for 24,725 shares at an exercise price of $9.10 per share, with a ten-year life, expiring April 28, 2027 (“April 2017 Warrants”).

Upon funding the second tranche of the Loan Agreement, the Company was obligated to issue warrants to purchase shares of the Company's common stock equal to 3.0% of the funded amount divided by an exercise price to be set based on the average price per share over the preceding 10 trading days prior to funding or the price per share prior to the day of funding. As such, the Company issued a second warrant for 41,736 shares at an exercise price of $5.39 per share with a ten-year life, expiring June 15, 2027 ("June 2017 Warrants").

The April 2017 Warrants and June 2017 Warrants issued were valued using the Black-Scholes option pricing model with the following assumptions: volatility of 71.42% and 71.57%, respectively, expected term of ten years, risk-free interest rate of 2.33% and 2.16%, respectively, and a zero-dividend yield. The collective 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.

Upon the funding of the tranche in connection with the Amendment, the Company was obligated to issue warrants to purchase shares of the Company's common stock equal to 1.0% of the funded amount divided by the exercise price to be set based on the average price per share over the preceding 10 trading days prior to closing. As such, the Company issued a warrant for 11,332 shares at an exercise price of $8.824 per share with a ten-year life, expiring December 4, 2028 ("December 2018 Warrants").

The December 2018 Warrants issued were valued using the Black-Scholes option pricing model with the following assumptions: volatility of 80.09%, expected term of ten years, risk-free interest rate of 2.98%, and a zero dividend yield. The collective warrant fair value of approximately $0.1 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, as amended and described above.

Summary of Carrying Value

The following table summarizes the components of the debt facility carrying value (in thousands):

	As of December 31, 2018	
	Short-term	Long-term
Principal payments to lender and end of term charge	$—	$ 25,033
Debt issuance costs	—	(268)
Debt discount related to warrants	—	(235)
Carrying value	$—	$ 24,530

The carrying value of the debt facility approximates fair value.

Future minimum payments under the debt facility are as follows (in thousands):

Year ending December 31,	
2019	$—
2020	2,000
2021	12,000
2022	12,500

Total future minimum payments	26,500
Unamortized end of term charge	(1,467)
Debt issuance costs and debt discount	(503)
Total minimum payment	24,530
Short-term portion	—
Long-term debt facility	$24,530

10. Fair Value Measurements

The Company measures and reports certain financial instruments at fair value on a recurring basis and evaluates its financial instruments subject to fair value measurements on a recurring basis to determine the appropriate level in which to classify them in each reporting period.

The Company determined that certain investments in debt securities classified as available-for-sale securities were Level 1 financial instruments.

Additional investments in corporate debt securities and commercial paper are considered Level 2 financial instruments because the Company has access to quoted prices, but does not have visibility to the volume and frequency of trading for all of these investments. For the Company's investments, a market approach is used for recurring fair value measurements and the valuation techniques use inputs that are observable, or can be corroborated by observable data, in an active marketplace.

Foreign exchange derivatives not designated as hedging instruments are considered Level 2 fair value measurements. The Company's foreign exchange derivative instruments are typically short-term in nature.

The Company also determined that the contingent consideration, described further below, was a Level 3 financial instrument.

The fair value of these instruments as of December 31, 2018 and 2017 was as follows (in thousands):

	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
As of December 31, 2018:			
Cash equivalents:			
U.S. Treasury money market funds	$14,710	$ —	$ —
Commercial paper	—	4,411	—
Corporate securities	—	2,371	—
Short-term investments:			
U.S. government securities	$15,965	$ —	$ —
Asset backed securities	—	8,588	—
Corporate securities	—	19,954	—
Commercial paper	—	42,022	—
Liabilities:			
Contingent consideration	$—	$ —	$ 12,214
Foreign exchange derivatives not designated as hedging instruments	—	26	—
As of December 31, 2017:			
Cash equivalents:			
U.S. Treasury money market funds	$4,540	$ —	$ —
Commercial paper	—	1,029	—
Repurchase agreements	—	2,500	—
Short-term investments:			
U.S. government securities	$11,885	$ —	$ —

Asset backed securities	—	8,383	—
Corporate securities	—	22,082	—
Commercial paper	—	29,842	—
Other assets:			
Foreign exchange derivatives not designated as hedging instruments	$—	$ 40	$ —
Liabilities:			
Contingent consideration	$—	$ —	$ 11,948

Pursuant to the acquisition of certain assets, liabilities, and subsidiaries of Serendex (see Note 2), Savara agreed to pay the seller, in addition to a set amount of shares of Savara's common stock, (i) $5 million upon receipt of marketing approval of Molgradex (the "Product") by the European Medicines Agency, (ii) $15 million upon receipt of marketing approval of the Product by the FDA, and (iii) $1.5 million upon receipt of marketing approval of the Product by the Japanese Pharmaceuticals and Medical Devices Agency (the "Contingent Milestone Payments"). The Company estimates the likelihood of approval in each region, separately, based on the product candidate's current phase of development and utilizing published studies of clinical development success rates for comparable non-oncology orphan drugs. The present value of the potential cash outflows from the probability weighted Contingent Milestone Payments is then estimated by taking into consideration that the Contingent Milestone Payments are similar to a business expense of the Company and would be senior to any Company debt obligations. The resulting weighted-average present value factor is then applied to discount the probability adjusted Contingent Milestone Payments for each region to derive the fair value of the Contingent Milestone Payments.

The following table sets forth a summary of the changes in the fair value of the Company's Level 3 financial instrument for the year ended December 31, 2018 and 2017 (in thousands):

	Warrant Liability	Put Options on 2017 Note	Contingent Consideration
Balance at December 31, 2016	$ 303	$ 979	$ 9,708
Change in fair value	67	169	2,240
Put option at issuance of 2017 Notes	—	828	—
Reclassification of warrant liability to common equity upon Merger	(370)	—	—
Conversion of convertible promissory notes upon Merger	—	(1,976)	—
Balance at December 31, 2017	$ —	$ —	$ 11,948
Change in fair value	—	—	266
Balance at December 31, 2018	$ —	$ —	$ 12,214

The Company records changes in fair value of the contingent consideration in general and administrative expense. In June 2017, the Company determined that there would be a change to the Molgradex program due to the FDA's guidance on the clinical program requirements for a New Drug Application submission in the U.S. related to the Molgradex product, which was issued in May 2017. Based on the FDA's guidance, the Company modified certain criteria of its Molgradex development program, which the Company believes will accelerate the development timeline in the U.S. The Company accordingly accounted for this change in its valuation of the contingent consideration as of June 30, 2017. Additionally, in the first quarter of 2018, Savara received approval from the FDA of its expansion of the Molgradex Phase 3 Study for aPAP into the U.S. to support its expedited U.S. development strategy for Molgradex. However, in order to achieve sufficient support for the study endpoints and outcome, the sample size of the study was increased, resulting in the extension of the patient enrollment completion dates, and hence, the approval dates of Molgradex, by approximately two calendar quarters. The Company likewise accounted for this change in its valuation of the contingent consideration in the requisite calendar quarters.

11. Derivative Financial Instruments

In the normal course of business, the Company is exposed to the impact of foreign currency fluctuations. The Company seeks to limit these risks by following risk management policies and procedures, including the use of derivatives. The Company's derivative contracts, which are not designated as hedging instruments, principally address short-term foreign currency exchange. The estimated fair value of the derivative contracts was based upon the relative exchange rate as of the balance sheet date. Accordingly, any gains or losses resulting from variances between this exchange rate at the contract inception date were recognized as "Other income or (expense)" in the consolidated statements of operations and comprehensive loss. As of December 31, 2018, there were approximately $3.1 million of unsettled forward exchange contracts to purchase foreign currency, a corresponding liability of approximately $3.1 million consisting of forward exchange contract obligations, resulting in minimal net derivative financial instruments, recorded at their estimated fair value in "Accrued expenses and other current liabilities."

12. Shareholders' Equity

Public Offerings

On June 7, 2017, the Company completed an underwritten public offering consisting of 9,034,210 shares of its common stock, which included 613,157 shares upon the partial exercise of the underwriters' option to purchase additional shares of Savara common stock at the public offering price, less the underwriting discounts and commissions. The net proceeds from the offering, after deducting the underwriting discounts and commissions and offering expenses, were approximately $39.5 million. The public offering was executed under an existing shelf registration statement as previously filed with the Securities and Exchange Commission on August 12, 2015 and declared effective on August 19, 2015.

On October 27, 2017, the Company completed an underwritten public offering consisting of 6,037,500 shares of its common stock, which included 787,500 shares upon the exercise of the underwriters' option to purchase additional shares of Savara common stock at the public offering price, less the underwriting discounts and commission, and pre-funded warrants to purchase 775,000 shares of Savara's common stock. The net proceeds from the offering, including the option to purchase additional shares, after deducting the underwriting discounts and commissions and offering expenses, were approximately $50.0 million. The public offering was executed under an existing shelf registration statement as previously filed with the Securities and Exchange Commission on August 12, 2015 and declared effective on August 19, 2015.

On July 30, 2018, the Company completed an underwritten public offering consisting of 4,250,000 shares of its common stock at a price to the public of $11.50 per share. The net proceeds from the offering, after deducting the underwriting discounts and commissions and offering expenses, were approximately $45.8 million. The July 2018 public offering was executed under a new shelf registration agreement filed with the Securities and Exchange Commission on June 29, 2018 and declared effective on July 13, 2018 (the "New Registration Statement").

The Company have used and intends to use the net proceeds from these offerings for working capital and general corporate purposes, which include, but are not limited to, the funding of clinical development of and pursuing regulatory approval for our product candidates, the initiation of Molgradex pre-commercialization activities, and general and administrative expenses.

Common Stock Sales Agreement

On April 28, 2017, the Company entered into a Common Stock Sales Agreement with H.C. Wainwright & Co., LLC ("Wainwright"), as sales agent, which was amended by Amendment No. 1 to the Common Stock Agreement (the "Amendment") on June 29, 2018 (the "Sales Agreement"), pursuant to which the Company may offer and sell, from time to time, through Wainwright, shares of Savara's common stock, par value $0.001 per share (the "Shares"), having an aggregate offering price of not more than $60.0 million, in addition to the $2.3 million in shares sold prior to the Amendment. The Amendment was effective on July 13, 2018, at the time the New Registration Statement was declared effective by the Securities and Exchange Commission. The Shares will be offered and sold pursuant to the New Registration Statement. Subject to the terms and conditions of the Sales Agreement, Wainwright will use its commercially reasonable efforts to sell the Shares from time to time, based upon the Company's instructions. The Company has provided Wainwright with customary indemnification rights, and Wainwright will be entitled to a commission at a fixed commission rate equal to 3.0% of the gross proceeds per Share sold. Sales of the Shares, if any, under the Sales Agreement may be made in transactions that are deemed to be "at the market offerings" as defined in Rule 415 under the Securities Act of 1933, as amended. The Company has no obligation to sell any of the Shares and may at any time suspend sales under the Sales Agreement or terminate the Sales Agreement.

During the years ended December 31, 2018 and 2017, the Company sold 48,600 and 198,298 shares of common stock under the Sales Agreement for net proceeds of approximately $0.5 million and $1.7 million, respectively.

Common Stock

The Company's amended and restated certificate of incorporation, as amended in June 2018, authorizes the Company to issue 201 million shares of common and preferred stock, consisting of 200 million shares of common stock with $0.001 par value and one million shares of preferred stock with $0.001 par value. The following is a summary of the Company's common stock at December 31, 2018 and 2017.

	December 31	
	2018	2017
Common stock authorized	200,000,000	500,000,000
Common stock outstanding	35,146,096	30,509,522

The Company's shares of common stock reserved for issuance as of December 31, 2018 and 2017 were as follows:

	December 31,	
	2018	2017
Warrants from Mast acquired in Merger	750,840	1,152,231
Warrants converted pursuant to Merger	72,869	74,992
April 2017 Warrants	24,725	24,725
June 2017 Warrants	41,736	41,736
December 2018 Warrants	11,332	—
Pre-funded warrants	775,000	775,000
Stock options outstanding	3,077,264	1,916,832
Issued and nonvested RSU's	156,250	86,875
Total shares reserved	4,910,016	4,072,391

Redeemable Convertible Preferred Stock

Prior to the Merger and the effect of the Exchange Ratio, the Company had 11,927,875 issued and outstanding shares of preferred stock, of which 1,799,906 shares were designated as Series A redeemable convertible preferred stock ("Series A"), 5,675,387 shares were designated as Series B redeemable convertible preferred stock ("Series B"), and 4,452,582 shares were designated as Series C redeemable convertible preferred stock ("Series C").

In the Merger, the previously outstanding shares of Series A and Series B preferred stock were converted on a one-to-one basis into shares of common stock and then subject to the Exchange Ratio. Due to the conversion of the 2016 Notes and 2017 Notes upon the Merger, the holders of Series C preferred stock received broad-based weighted-average anti-dilution protection such that the previously outstanding shares of Series C preferred stock were converted on a 1:1.017 basis (the "Anti-Dilution Conversion Ratio") into shares of common stock and then adjusted for the Exchange Ratio. Following the Merger, there were no shares of preferred stock outstanding.

No dividends on the convertible preferred stock were declared by the Board of Directors from inception through their conversion into common stock.

Warrants

Immediately prior to the Merger, Series B Warrants were exercised and exchanged for 111,799 shares of the Company's common stock after giving effect to the Exchange Ratio. Proceeds from the cash exercises were $0.4 million.

In connection with the Merger, Series C Warrants were converted to warrants to purchase 74,992 shares of the Company's common stock after giving effect to both the Anti-Dilution Conversion Ratio and Exchange Ratio.

The following table summarizes the outstanding warrants for the Company's common stock as of December 31, 2018:

Shares Underlying Outstanding Warrants	Exercise Price	Expiration Date
314,446	$ 52.50	November 2019
32,467	$ 7.00	August 2020
403,927	$ 29.40	February 2021
72,869	$ 8.98	June 2021
775,000	$ 0.01	October 2024
24,725	$ 9.10	April 2027
41,736	$ 5.39	June 2027
11,332	$ 8.824	December 2028
1,676,502		

Beneficial Conversion Feature

Due to the conversion of the 2016 Notes and 2017 Notes upon the Merger and the effect of the Anti-Dilution Conversion Ratio to the holders of Series C preferred stock and Series C Warrants, a Contingent Beneficial Conversion Feature ("BCF") was triggered resulting in an intrinsic BCF value attributable to the securities of approximately $0.4 million, collectively. Since the conversion of the Series C preferred stock and Series C Warrants occurred contemporaneously on the BCF commitment date, the Company measured the value on that date and recorded the BCF as a "deemed dividend" in the year ended December 31, 2017.

Financial Advisor Fees

The Company executed an agreement with Canaccord Genuity in February 2016, as modified in March 2017, where Savara was obligated to pay Canaccord Genuity a success fee upon the closing of the Merger. Pursuant to the Merger and public offering on June 7, 2017, the Company paid Canaccord Genuity $1.0 million in July 2017 related to the success fee.

13. Commitments

Operating Leases

We are obligated under operating leases for office space. On November 29, 2017, we entered into a sublease agreement for a new office space for our corporate headquarters in Austin, Texas. The term of the sublease for the new space commenced on January 1, 2018 and will continue until July 31, 2021, with annual rental payments of approximately $0.2 million, paid over monthly installments, subject to increases of approximately 2% annually on the anniversary of the commencement date of the sublease term. However, monthly base rent for the first month of the sublease term was abated. We recently leased new office space in Copenhagen, Denmark with a lease effective on November 1, 2018 and expiring on September 30, 2022. Our annual rent is approximately $0.1 million, paid over monthly installments, subject to annual increases varying from 2.5% to 5.0%. On March 23, 2017, we sublet office space located in San Diego, California with rentable office space of approximately 13,707 square feet, which previously served as Mast's corporate headquarters, to a third party. However, as a result of the Merger, the Company no longer had an ongoing need for this facility. The term of the sub-sublease commenced on July 1, 2017 and expires on May 31, 2020, coterminous with a sublease agreement dated June 19, 2014 with the sublessor. As of December 31, 2018, annual rent under the sub-sublease is approximately $0.5 million, payable in monthly installments.

We previously leased office space for our corporate headquarters, prior to our relocation on January 1, 2018, discussed herein, in Austin, Texas, pursuant to an operating lease dated November 19, 2012, as amended May 22, 2015 under which we are obligated to remit annual rental payments of approximately $0.1 million payable in monthly installments for the period January 1, 2018 through November 30, 2019. On November 29, 2017, we entered into a sublease agreement pursuant to which the sublessee assumed the office space and rental payments effective January 1, 2018 through November 30, 2019 except for the first month rent on January 2018.

The future minimum annual lease payments under the operating leases are as follows (in thousands):

Year ending December 31,	
2019	$843
2020	471
2021	175
2022	60
Total future minimum lease payments	$1,549

Rent expense for our office spaces is recognized on a straight-line basis. Rent expense for the years ended December 31, 2018 and 2017 was $0.3 million and $0.3 million, respectively, and reflected an offset of sublessee rental receipts.

As of December 31, 2018, the Company leases certain research and development equipment as part of a contract manufacturing arrangement. The leased equipment is accounted for as a capital lease, and the present value of the future minimum lease payments are recorded as a liability on the balance sheet as of December 31, 2018. The future minimum annual lease payments under the capital lease are as follows (in thousands):

Year ending December 31,	
2019	$45
Total minimum lease payments	45

Less: imputed interest	(4)
Total capital lease obligation	$41

Contingent Royalty and Milestone Payments

The Company is also subject to certain contingent royalty payments to the Cystic Fibrosis Foundation as further described below, and certain manufacturers of Molgradex and related suppliers as described in Note 2.

CFF Award

In September 2013, the Company received a $1.7 million award (the "CFF Award") from the Cystic Fibrosis Foundation ("CFF") related to the development of the Company's AeroVanc product. The CFF Award includes disbursements to the Company based upon the achievement of certain milestones. If the milestone payments are achieved, requested, and received by the Company, Savara is then subject to these royalty payments, due to the CFF, as follows: (i) based on commercialization of AeroVanc an amount equal to three (3) times the amount of the CFF Award; (ii) upon the achievement of net sales exceeding $50.0 million for any calendar year during the first five years after the first commercial sale, an amount equal to one (1) times the amount of the CFF Award; (iii) upon the achievement of net sales exceeding $100.0 million for any calendar year during the first five years after the first commercial sale, an amount equal to one (1) times the amount of the CFF Award; (iv) upon a change in control transaction, as defined in the CFF Award agreement, occurring prior to the second anniversary date of the effective date of the CFF Award, September 30, 2015, an amount equal to 5% of the proceeds from the change in control transaction but not to exceed an amount equal to two (2) times the CFF Award proceeds received; and (v) upon a change in control transaction occurring after the second anniversary date of the effective date of the CFF Award, an amount equal to 5% of the proceeds from the change in control transaction or a sale or license of the AeroVanc program with a third party but not to exceed an amount equal to (3) three times the CFF Award.

Since the Company has earned the full amount of the CFF Award, or $1.7 million, during the periods preceding the years ended December 31, 2018 and 2017, it recognized grant revenue in the requisite prior periods accordingly and is subject to the royalty obligations described above as calculated on the full amount of the CFF Award received, or $1.7 million. However, as the Company has not recognized any sales from AeroVanc, the Company has not recorded a liability for any amounts due as additional royalties.

On November 28, 2017, Savara entered into an amended agreement to the CFF Award ("Amended CFF Award"), pursuant to which the amount of the development award available to Savara was increased by $5.0 million to an aggregate of $6.7 million. Pursuant to the terms of the Amended CFF Award, if Savara elects to draw down funds on the increased award, it is obligated to make royalty payments to CFF as follows: (i) based on commercialization of AeroVanc an amount equal to four (4) times the amount Savara receives under the Amended CFF Award; (ii) upon the achievement of net sales exceeding $50.0 million for any calendar year during the first five years after the first commercial sale, a payment equal to the amount Savara receives under the Amended CFF Award; (iii) upon the achievement of net sales exceeding $100.0 million for any calendar year during the first seven years after the first commercial sale, a payment equal to the amount Savara receives under the Amended CFF Award; and (iv) upon the consummation of a change of control transaction, as defined in the Amended CFF Award agreement, or a sale or license of the AeroVanc program with a third party, an amount equal to 7.5% of the amount received from the third party in connection with such transaction, up to a total of four (4) times the amount received by Savara under the Amended CFF Award with any such payments credited against the royalty payments due upon commercialization of AeroVanc, and under which Savara must continue paying or cause the third party to assume any remaining royalties payable to CFF pursuant to the Amended CFF Award.

As of December 31, 2018 and 2017, the Company had made no draws against the Amended CFF Award.

Risk Management

The Company maintains various forms of insurance that the Company's management believes are adequate to reduce the exposure to these risks to an acceptable level.

Employment Agreements

Certain executive officers are entitled to payments if they are terminated without cause or resign for good reason (each as defined in the employment agreements). Upon termination without cause, and not as a result of death or disability,

or resignation for good reason, each of such officers is entitled to receive a payment of base salary for twelve months and a pro-rated portion of their unpaid bonus following termination of employment, and such officer will be entitled to continue to receive coverage under medical and dental benefit plans for twelve months or until such officer is covered under a separate plan from another employer. Upon a termination other than for cause or resignation for good reason within twelve months following a change in control, each of such officers is entitled to receive a payment of base salary for eighteen months and one-hundred percent of their unpaid bonus following termination of employment and such officer will be entitled to continue to receive coverage under medical and dental benefit plans for twelve months or until such officer is covered under a separate plan from another employer and will also be entitled to certain acceleration of such officer’s outstanding nonvested options at the time of such termination.

14. Related Party Transactions

Pursuant to the Company's public offering on June 7, 2017 (Note 12), Zambon SpA ("Zambon") purchased 4,693,540 shares of the Company's common stock resulting in ownership of approximately 13.4% and 15.4% of the Company's outstanding shares and voting interests as of December 31, 2018 and 2017, respectively. Due to the aforementioned percentage ownership of the Company's common stock, Zambon is thereby considered a related party to the Company for the years ended December 31, 2018 and 2017.

15. Stock-Based Compensation

A. 2008 Stock Option Plan

The Company adopted the Savara Inc. Stock Option Plan (the "2008 Plan"), pursuant to which the Company had reserved shares for issuance to employees, directors, and consultants. The 2008 Plan includes (i) the option grant program providing for both incentive and non-qualified stock options, as defined by the Internal Revenue Code, and (ii) the stock issuance program providing for the issuance of awards that are valued based upon common stock, including restricted stock, dividend equivalents, stock appreciation rights, phantom stock, and performance units. The 2008 Plan also allows eligible persons to purchase shares of common stock at an amount determined by the plan administrator. Upon a participant's termination, the Company retains the right to repurchase nonvested shares issued in conjunction with the stock issuance program at the fair market value per share as of the date of termination.

Prior to the closing of the Merger, the Company had issued incentive and non-qualified options and restricted stock to employees and non-employees under the 2008 Plan. The terms of the stock options, including the exercise price per share and vesting provisions, were determined by the board of directors. Stock options were granted at exercise prices not less than the estimated fair market value of the Company's common stock at the date of grant based upon objective and subjective factors including: third-party valuations, preferred stock transactions with third parties, current operating and financial performance, management estimates and future expectations. Stock option grants typically vest quarterly over three to four years and expire ten years from the grant date, and restricted stock grants typically vest on a quarterly basis over four years and expire ten years from the grant date.

Changes in 2008 Plan

Subsequent to the Merger, the Company no longer issues awards under the 2008 Plan.

B. 2015 Omnibus Incentive Option Plan

The Company operates the 2015 Omnibus Incentive Plan (the "2015 Plan"), which was amended and approved by stockholders in June 2018. The 2015 Plan provides for the grant of incentive and non-statutory stock options, as well as share appreciation rights, restricted shares, restricted stock units ("RSUs"), performance units, shares and other stock-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, 2018, the number of shares of our common stock available for grant under the 2015 Plan was 1,588,518 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 restricted stock right such as an RSU. 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.

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 Options and Restricted Stock Units

The Company values stock options using the Black-Scholes option pricing model, which requires the input of subjective assumptions, including the risk-free interest rate, expected life, expected stock price volatility and dividend yield. The risk-free interest rate assumption is based upon observed interest rates for constant maturity U.S. Treasury securities consistent with the expected term of the Company's employee stock options. The expected life represents the period of time the stock options are expected to be outstanding and is based on the simplified method. The Company uses the simplified method due to the lack of sufficient historical exercise data to provide a reasonable basis upon which to otherwise estimate the expected life of the stock options. Expected volatility is based on historical volatilities for publicly traded stock of comparable companies over the estimated expected life of the stock options. The Company assumes no dividend yield because dividends are not expected to be paid in the near future, which is consistent with the Company's history of not paying dividends. The valuation of stock options is also impacted by the valuation of common stock. Stock option awards generally have ten-year contractual terms and vest over four years for issuances to employees based on continuous service; however, the 2015 Plan allows for other vesting periods.

Fair Value Assumptions for 2008 Plan and 2015 Plan

The following table summarizes the assumptions used for estimating the fair value of stock options granted to employees for the years ended December 31, 2018 and 2017:

	2018	2017
Risk-free interest rate	2.75% - 3.09%	2.08% - 2.24%
Expected term (years)	7.05	7.05
Expected volatility	79% - 81%	80% - 81%
Dividend yield	0%	0%

The following table summarizes the assumptions used for estimating the fair value of stock options granted to non-employees for the year ended December 31, 2018 and 2017:

	2018	2017
Risk-free interest rate	2.82%	1.97% - 2.39%
Expected term (years)	7.05	7.05 - 9.82
Expected volatility	80%	80%
Dividend yield	0%	0%

C. Stock-Based Award Activity

The following tables provides a summary for the 2008 Plan and 2015 Plan of stock option activity for employees and non-employees, restricted stock, and RSU activity for the year ended December 31, 2018 after giving effect to the Exchange Ratio:

Stock Options:

	Shares Underlying Option Awards	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life	Aggregate Intrinsic Value (in 000's)
Outstanding at December 31, 2017	1,916,832	$ 3.47	7.89	$ 22,504
Granted	1,470,420	9.99	7.05	
Exercised	(186,138)	0.89		
Expired/cancelled/forfeited	(123,850)	15.02		
Outstanding at December 31, 2018	3,077,264	$ 6.28	8.30	$ 7,975
Options exercisable at December 31, 2018	1,292,671	$ 3.76	7.11	$ 5,687
Vested and expected to vest at December 31, 2018	3,077,264	$ 6.28	8.30	$ 7,975

RSUs:

	Shares Underlying Option Awards	Weighted-Average Grant Date Fair Value
Outstanding at December 31, 2017	86,875	$ 7.08
Granted	120,000	11.33
Exercised	(50,625)	9.41
Expired/cancelled/forfeited	—	—
Outstanding at December 31, 2018	156,250	$ 9.59

Restricted Stock:

The following table summarizes the restricted stock activity for the years ended December 31, 2018 and 2017:

	Restricted Shares	Weighted-Average Grant Date Fair Value
Nonvested at December 31, 2016	108,411	$ 0.69
Granted	—	—
Vested	(73,176)	0.74
Forfeited	(19,045)	0.50
Nonvested at December 31, 2017	16,190	$ 0.65
Granted	—	—
Vested	(16,190)	0.65
Forfeited	—	—
Nonvested at December 31, 2018	—	$ —

The total fair value of restricted stock that vested during the year ended December 31, 2018 was $0.2 million. As of December 31, 2018, there was no remaining compensation cost related to nonvested restricted stock not yet recognized.

During the years ended December 31, 2018 and 2017, the Company did not issue any shares of restricted stock to employees under the 2008 Plan.

The following table provides a summary of options issued to employees and non-employees that are outstanding and vested as of December 31, 2018:

Exercise Price	Number Outstanding	Weighted-Average Life (in Years)	Number Exercisable	Weighted-Average Life (in Years)
$ 0.19	22,854	0.14	22,854	0.14
$ 0.31	7	0.95	7	0.95
$ 0.52	29,774	1.96	29,774	1.96
$ 0.55	10,036	2.96	10,036	2.96
$ 0.65	181,527	5.03	181,527	5.03
$ 0.82	101,378	5.00	101,378	5.00
$ 1.46	443,863	6.97	336,917	6.97
$ 1.51	95,684	7.82	31,895	7.82
$ 1.76	501,177	7.96	254,885	7.96
$ 5.13	7,500	8.40	7,500	8.40
$ 5.85	15,000	8.50	4,688	8.50
$ 7.33	433,700	9.96	3,750	9.96
$ 8.70	88,000	8.79	21,750	8.80
$ 9.93	10,000	9.36	1,250	9.36
$ 10.01	20,000	9.81	—	9.81
$ 11.26	985,000	9.59	245,625	9.59
$ 11.33	10,000	9.19	2,143	9.19
$ 15.21	121,764	8.97	36,692	8.97
	3,077,264		1,292,671	

The weighted-average grant date fair values for the Company's stock options granted during the years ended December 31, 2018 and 2017 were $10.07 per share and $9.11 per share, respectively. The total compensation cost related to nonvested stock options not yet recognized as of December 31, 2018 was $10.3 million, which will be recognized over a weighted-average period of approximately 3.07 years. Stock options to purchase 186,138 shares and 124,061 shares were exercised during the years ended December 31, 2018 and 2017, respectively.

During the years ended December 31, 2018 and 2017, the Company granted options to purchase a total of 0 and 10,000 shares of common stock to non-employees, respectively, under the 2015 Plan.

The Company recorded a minimal amount of stock-based compensation expense for options issued to non-employees for the years ended December 31, 2018 and 2017, respectively. As of December 31, 2018, options to purchase 4,665 shares were held by non-employee and were vested and outstanding.

D. Stock-Based Compensation

Stock-based compensation expense is included in the following line items in the accompanying statements of operations and comprehensive loss for the years ended December 31, 2018 and 2017 (in thousands):

	Year ended December 31,	
	2018	2017
Research and development	$1,626	$207
General and administrative	2,111	345
Total stock-based compensation	$3,737	$552

16. License Agreement

The Company entered into a license agreement on May 12, 2016, as amended on June 4, 2018 (the "License Agreement"), with a licensee under which the licensee received an exclusive right to import, market, sell, distribute and promote Molgradex in Japan for the treatment of aPAP. In return, the licensee will pay the Company marketing and regulatory-based milestone payments and sales-based royalties. In October 2018, the Company achieved a milestone payment pursuant to the License Agreement resulting in the receipt of $0.3 million from the licensee. As of December 31, 2018, the Company has determined that it has not met all of the performance obligations under the License Agreement and, accordingly, has recorded the milestone payment as deferred revenue in "Accrued expenses and other current liabilities" in the Company's consolidated balance sheet until such time the performance obligations are met.

17. Income Taxes

The components of loss before income taxes for the years ended December 31, 2018 and 2017 are as follows (in thousands):

	December 31,	
	2018	2017
Domestic	$(48,868)	$(21,942)
Foreign	(21,159)	(11,489)
Total	$(70,027)	$(33,431)

The Company recorded a federal tax benefit of approximately $4.6 million for income tax during the year ended December 31, 2018 due to the reduction of its deferred tax liability related to the impairment and corresponding decrease to the carrying value of IPR&D associated with the Aironite drug candidate assumed in the Merger (as defined and further described in Note 7). During the year ended December 31, 2017, the Company recorded a federal tax benefit of $2.8 million for income tax related to a rate reduction on a deferred tax liability. The Company recorded no state provision for income taxes for the years ended December 31, 2018 and 2017, due to revenues below the minimum tax threshold. The Company recorded a foreign current income tax benefit related to the refundable research credits (as defined and further described in Note 2). The components of the benefit for income taxes are as follows for the years ended December 31, 2018 and 2017 (in thousands):

	December 31,	
	2018	2017
Current:		
Federal	$—	$—
State	—	—
Foreign	(1,330)	(814)
Total Current	(1,330)	(814)
Deferred:		
Federal	(4,555)	(2,820)
State	—	—
Foreign	(2,626)	—
Total Deferred	(7,181)	(2,820)
Total income tax expense (benefit)	$(8,511)	$(3,634)

A reconciliation of the expected income tax benefit computed using the federal statutory income tax rate to the Company's effective income tax rate is as follows for the years ended December 31, 2018 and 2017 (in thousands):

	December 31,	
	2018	2017
Income tax expense (benefit) computed at federal statutory tax rate	$(14,706)	$(11,367)
Change in valuation allowance	8,692	1,487
Orphan drug & research credits generated	(4,399)	(3,427)
Orphan drug & research credit expense disallowance	1,164	1,691
Contingent liability	56	762
Impact of foreign operations	(305)	1,363
Note conversion	—	618
Change in tax rate due to the 2017 Tax Act	—	4,096
Transaction costs	—	657
Other permanent differences	987	486
Total	$(8,511)	$(3,634)

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The Company has

established a valuation allowance due to uncertainties regarding the realization of deferred tax assets based upon the Company's lack of earnings history. During the years ended December 31, 2018 and 2017, the valuation allowance increased by $8.7 million and $7.9 million, respectively.

Significant components of the Company's deferred tax assets and liabilities are as follows (in thousands):

	December 31,	
	2018	2017
Deferred tax liabilities:		
Depreciation	$14	$87
Prepaid assets	—	378
Intangible assets	2,845	7,181
Other	237	—
Total deferred tax liabilities	3,096	7,646
Deferred tax assets:		
Net operating loss carryforwards	21,406	13,194
Amortization	208	6
Credit carryforwards	12,706	9,770
Accrued liabilities & other	318	345
Total deferred tax assets	34,638	23,315
Subtotal	31,542	15,669
Valuation allowance	(31,542)	(22,850)
Net deferred taxes	$—	$(7,181)

On December 22, 2017, the President signed into law the Tax Cuts and Jobs Act (the "Tax Act"), reducing the U.S. corporate income tax rate to 21% effective January 1, 2018. Under ASC 740 "Income Taxes," the effects of new legislation are recognized in the period that includes the date of enactment.

Subsequent to the enactment of the Tax Act, the SEC staff issued Staff Accounting Bulletin No. 118, "Income Tax Accounting Implications of the Tax Cuts and Jobs Act," which allows companies to record provisional amounts related to the effects of the Tax Act to the extent that a company's accounting for certain income tax effects of the Tax Act is incomplete but the company is able to determine a reasonable estimate during a measurement period not to extend beyond one year from the enactment date. The Company previously made provisional estimates for the impact of the Tax Act as of and for the year ended December 31, 2017 related to the remeasurement of our deferred tax liability. The impact was to remeasure our deferred tax liability by $2.8 million as of December 31, 2017, which has been reflected in our effect tax rate reconciliation. As of December 31, 2018, we have completed our accounting and measurement analyses related to the income tax effects of the Tax Act, and no significant adjustments to the provisional amounts were recorded during the year ended December 31, 2018.

As of December 31, 2018 and 2017, the Company had foreign net operating loss ("NOL") carryforwards of approximately $23.1 million $9.5 million, respectively, which have an indefinite carryforward period. During the fourth quarter of 2018, the Company corrected its accounting to include deferred tax liabilities related to indefinite lived in-process research and development assets as a source of income in determining the realizability of net operating losses with an indefinite carryforward period. The Company has recorded a tax benefit of $2.5 million in the fourth quarter of 2018 related to the reduction of the valuation allowance on deferred tax assets related to net operating losses with an indefinite carryforward period of which $1.8 million relates to annual periods prior to 2018. The Company believes the adjustment is not material to the current or prior annual or interim periods. As of December 31, 2018 and 2017, the Company had NOL's for federal income tax purposes of approximately $77.7

million and $52.8 million, respectively. As of December 31, 2018 and 2017, the Company also had available research and orphan drug tax credit carryforwards for federal income tax purposes of approximately $12.5 million and $9.7 million, respectively. If not utilized, these carryforwards expire at various dates beginning in 2028. As of December 31, 2018 and 2017, the Company had state research and development tax credit carryforwards of approximately $0.3 million and $0.1 million, respectively, which will begin to expire in 2034 if not utilized.

Utilization of the NOL and tax credit carryforwards may be subject to an annual limitation due to ownership change limitations that have occurred previously or that could occur in the future, as provided by Section 382 of the Internal Revenue Code of 1986 (“Section 382”), as well as similar state provisions. Ownership changes may limit the amount of NOL carryforwards and tax credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an ownership change, as defined by Section 382, results from transactions that increase the ownership of 5% shareholders in the stock of a corporation by more than 50 percentage points in the aggregate over a three-year period. The Company has not performed a study to determine whether any ownership change has occurred since the Company’s formation through December 31, 2018. However, the Company believes that it has experienced at least two ownership changes in the past and that it may experience additional ownership changes as a result of subsequent shifts in its stock ownership. Should there be an ownership change that has occurred or will occur, the Company’s ability to utilize existing carryforwards could be substantially restricted and may result in the expiration of such carryforwards prior to utilization.

The Company applies the accounting guidance in ASC 740 related to accounting for uncertainty in income taxes. The Company's reserves related to taxes are based on a determination of whether, and how much of, a tax benefit taken by the Company in its tax filings or positions is more likely than not to be realized following resolution of any potential contingencies present related to the tax benefit. As of December 31, 2018 and 2017, the Company had no unrecognized tax benefits. During the years ended December 31, 2018 and 2017, the Company had no interest and penalties related to income taxes.

The Company files income tax returns in the U.S. federal, state, and foreign jurisdictions. As of December 31, 2018, the statute of limitations for assessment by the Internal Revenue Service ("IRS") is open for the 2015 and subsequent tax years, although carryforward attributes that were generated for tax years prior to then may still be adjusted upon examination by the IRS if they either have been, or will be, used in a future period. The 2014 and subsequent tax years remain open and subject to examination by the state taxing authorities. The 2017 and subsequent tax years remain open and subject to examination by the foreign taxing authorities. There are currently no federal, state, or foreign income tax audits in progress.

18. Net Loss per Share

Basic net loss per share is computed by dividing the net loss by the weighted-average number of common shares outstanding. Diluted net loss per share is computed similarly to basic net loss per share except that the denominator is increased to include the number of additional common shares that would have been outstanding if the potential common shares had been issued and if the additional common shares were dilutive. Diluted net loss per share is the same as basic net loss per common share, since the effects of potentially dilutive securities are antidilutive.

As of December 31, 2018 and 2017 potentially dilutive securities include:

	Year ended December 31,	
	2018	2017
Awards under equity incentive plan	3,077,264	1,916,832
Nonvested restricted shares and restricted stock units	156,250	103,065
Warrants to purchase common stock	901,502	2,068,684
Total	4,135,016	4,088,581

The following table reconciles basic earnings per share of common stock to diluted earnings per share of common stock for the years ended December 31, 2018 and 2017 (in thousands, except share and per share amounts):

	Year ended December 31,	
	2018	2017
Net loss	$(61,516)	$(29,797)
Accretion of convertible redeemable preferred stock	—	(578)
Deemed dividend on beneficial conversion feature	—	(404)
Net loss attributable to common stockholders	$(61,516)	$(30,779)

Undistributed earnings and net loss attributable to common stockholders, basic and diluted	$(61,516)	$(30,779)
Weighted-average common shares outstanding, basic and diluted	33,300,704	17,521,119
Basic and diluted EPS	$(1.85)	$(1.76)

19. Quarterly Financial Data (Unaudited)

The following table summarizes unaudited quarterly financial data for the years ended December 31, 2018 and 2017 (in thousands, except per share amounts):

	2018			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Revenues	$—	$—	$—	$—
Operating loss	$(32,107)	$(11,906)	$(12,784)	$(13,248)
Net loss	$(26,849)	$(11,593)	$(12,560)	$(10,514)
Basic and diluted net loss per share*	$(0.86)	$(0.37)	$(0.36)	$(0.29)

	2017			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Revenues	$—	$—	$—	$—
Operating loss	$(4,774)	$(9,343)	$(6,543)	$(9,296)
Net loss	$(4,974)	$(11,504)	$(6,817)	$(6,502)
Basic and diluted net loss per share	$(0.97)	$(0.90)	$(0.28)	$(0.23)

* During the fourth quarter of 2018, the Company identified and corrected for pre-funded warrants that were excluded from the basic and diluted net loss per share calculation. The Company considered both quantitative and qualitative factors in assessing the impact of the exclusion of these pre-funded warrants to the calculation of basic and diluted net loss per share and concluded that the exclusion was not material to any prior periods presented. The Company has revised the basic and diluted net loss per share calculation for the three months ended March 31, 2018, June 30, 2018, and September 30, 2018 in the table above. The related impact was a reduction to the basic and diluted net loss per share calculations in the amount of two cents, one cent, and one cent for the three months ended March 31, 2018, June 30, 2018, and September 30, 2018, respectively.