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, 2019

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 001-36620

NOVUS THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware **(State or other jurisdiction of incorporation or organization)**	**20-1000967** **(I.R.S. Employer Identification No.)**
19900 MacArthur Boulevard, Suite 550 **Irvine, California** **(Address of principal executive offices)**	**92612** **(Zip code)**

(949) 238-8090

(Registrant's telephone number, including area code)

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

Title of Class	Trading Symbol(s)	Name of Exchange on Which Registered
Common Stock, $0.001 par value	**NVUS**	**Nasdaq Capital 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 Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

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

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

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

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

As of June 28, 2019, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the registrant's common stock held by non-affiliates was $9,638,037, based on the last reported sale price of such stock on the Nasdaq Global Market as of such date.

As of March 9, 2020, the registrant had 16,069,562 shares of Common Stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2020 Annual Meeting of Stockholders, which the registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year end December 31, 2019, are incorporated by reference into Items 10, 11, 12, 13 and 14 of Part III of this Annual Report on Form 10-K.

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In this Annual Report on Form 10-K, Annual Report, unless the context requires otherwise, "Novus", the "Company", "we", "our", and "us" means Novus Therapeutics, Inc. and all wholly owned subsidiaries.

Forward-Looking Statements

This Annual Report on Form 10-K contains "forward-looking statements" as defined by the Private Securities Litigation Reform Act of 1995, which statements involve substantial risks and uncertainties. Any statements in this Annual Report on Form 10-K about the Company's future expectations, plans and prospects, including statements about its strategy, future operations, development of its product candidates, the review of strategic alternatives and the outcome of such review and other statements containing words such as "believes," "anticipates," "plans," "expects," "estimates," "intends," "predicts," "projects," "targets," "could," "may," and similar expressions, constitute forward-looking statements, although not all forward-looking statements include such identifying words. Forward-looking statements include, but are not limited to statements regarding:

- expectations regarding the timing for the commencement and completion of product development or clinical trials for the Company's product candidates;
- the timing, costs, conduct and outcome of preclinical studies and clinical studies;
- meeting future clinical and regulatory milestones, such as New Drug Application ("NDA") submissions;
- the risk that clinical studies of the Company's product candidates may not be successful in establishing their safety and tolerability or efficacy;
- the Company's plans and timing with respect to seeking regulatory approvals and uncertainties regarding the regulatory process;
- the anticipated treatment of data by the U.S. Food and Drug Administration ("FDA"), the European Medicines Agency ("EMA") or other regulatory authorities of the Company's product candidates;
- the rate and degree of market acceptance and clinical utility of the Company's product candidates;
- the Company's commercialization, marketing and manufacturing capabilities and strategy;
- the Company's intellectual property position and strategy;
- the Company's ability to identify additional product candidates with significant commercial potential;
- the availability of funds and resources to pursue the Company's research and development projects, including preclinical studies and clinical studies of its product candidates;
- the Company's estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- the Company's ability to continue as a going concern;
- developments relating to the Company's competitors and industry;
- the impact of government laws and regulations;
- the duration over which the Company's cash balances will fund its operations; and
- those risk factors identified in this Annual Report on Form 10-K under the heading "Risk Factors" and in other filings the Company periodically makes with the SEC.

Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the ability to develop commercially viable product formulations; the sufficiency of the Company's cash resources; the ability to obtain necessary regulatory and ethics approvals to commence additional clinical trials; whether data from early clinical trials will be indicative of the data that will be obtained from future clinical trials; whether the results of clinical trials will warrant submission for regulatory approval of any investigational product; whether any such submission will receive approval from the FDA or equivalent foreign regulatory agencies and, if the Company is able to obtain such approval for an investigational product, whether it will be successfully distributed and marketed. These risks and uncertainties, as well as other risks and uncertainties that could cause the Company's actual results to differ significantly from the forward-looking statements contained herein, are described in greater detail in Part I, Item 1A. *Risk Factors* in this Annual Report on Form 10-K.

Any forward-looking statements contained in this Annual Report on Form 10-K speak only as of the date hereof and not of any future date, and the Company expressly disclaims any intent to update any forward-looking statements, whether as a result of new information, future events or otherwise.

The market data and certain other statistical information used in this Annual Report are based on independent industry publications, governmental publications, reports by market research firms or other independent sources. Some data are also based on our good faith estimates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information.

PART I

Item 1. Business.

Overview

Novus Therapeutics, Inc. is a specialty pharmaceutical company focused on developing products for patients with disorders of the ear, nose, and throat. The Company has two platform technologies, a surfactant and a foam, each with the potential to be developed for multiple indications. Novus' lead program, OP0201, is a surfactant-based nasal aerosol drug-device combination product candidate being developed as a potential first-in-class treatment option for patients at risk for, or with, otitis media ("OM"). OM is defined as middle ear inflammation and effusion with or without infection. Globally, OM affects more than 700 million adults and children every year, with over half of the cases occurring in children under five years of age. OM is one of the most common disorders seen in pediatric practice, and is a leading cause of health care visits and the most frequent reason children are prescribed antibiotics or undergo surgery in the United States. Novus also has a foam-based drug delivery technology platform, which may be developed in the future to deliver drugs into the ear, nasal, and sinus cavities.

Surfactant Platform

The first product candidate in the surfactant platform program, OP0201, is being developed as a potential first-in-class treatment option for OM. OM is often caused by Eustachian tube dysfunction ("ETD"). OP0201 is a nasal aerosol, drug-device combination product comprised of a novel formulation of a surfactant (dipalmitoylphosphatidylcholine ("DPPC")) and a spreading agent (cholesteryl palmitate ("CP")) suspended in propellant. The product is administered intranasally via a pressurized metered-dose inhaler ("pMDI"). OP0201 is intended to be used to restore the normal physiologic activity of the Eustachian tube ("ET"), which is a small tube that connects from the chamber of the middle ear to the back of the nasopharynx. Together, the active ingredients in OP0201 effectively absorb to the air-liquid interface of the mucosa and reduce the interfacial surface tension of the ET, which reduces passive pressure required for the ET to open. In other words, OP0201 promotes 'de-sticking' of the ET so that ventilation of the middle ear is restored. Novus is also exploring the use of a dry-powder unit dose device as an alternative option for intranasal administration of DPPC and CP.

Novus has completed three phase 1 placebo-controlled clinical trials in adults that were designed to evaluate safety and tolerability of single and repeated intranasal doses of OP0201. Results of a single-dose phase 1 trial in healthy adults (study C-001), a single-dose phase 1 trial in adults with acute otitis media (study C-004), and a 14-day phase 1 trial in healthy adults (study C-002) demonstrated the safety and tolerability of OP0201 nasal aerosol. Novus is currently conducting an exploratory phase 2a clinical trial of OP0201 nasal aerosol in infants and children with acute otitis media (study C-006).

Novus' surfactant development program, if successful, will lead to registration of a surfactant-based product in North America and key European markets to treat and/or prevent OM in infants and children. Additional development activities to support registration in other countries, or for other indications, or other patient populations, may occur in the future.

Foam Platform

Novus has two product candidates developed, OP0101 and OP0102, which are foam-based product candidates intended to be used as a delivery vehicle for drugs to be administered into the ear canals, as well as the nasal and sinus cavities. OP0101 foam otic was the initial product candidate utilizing the foam platform. It was developed as an improved treatment option for acute otitis externa ("AOE"), a common infectious medical condition of the outer ear canal that affects tens of millions of adults and children each year (frequently called "swimmer's ear"). Novus completed four clinical trials of OP0101 foam otic in 353 adult and pediatric subjects, including a successful phase 2b study with a steroid-free, antibiotic-only formulation of OP0101 foam otic that was non-inferior to standard of care, but with a more favorable dosing regimen (once a day dosing instead of twice a day).

OP0102 foam otic is a second-generation formulation designed to rapidly relieve ear pain (an unmet need in AOE) and eradicate infection with less than seven days of treatment. In May 2017, Novus suspended the foam otic platform development program to focus resources on the surfactant program.

Otitis Media (“OM”)

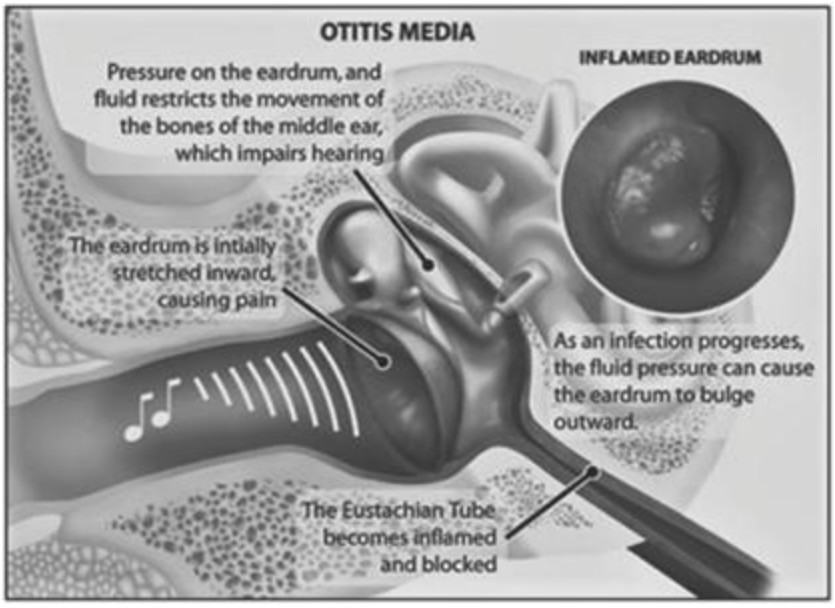
OM is a generic term without reference to a specific etiology or pathogenesis and best regarded as a spectrum of diseases of the middle ear. OM is a very common condition and a leading cause of healthcare visits and antibiotic prescriptions. Common forms of OM are acute OM (“AOM”) and otitis media with effusion (“OME”). Both AOM and OME can occur episodically or persist for long periods of time. If reoccurrence is frequent (e.g., three episodes within six months), the patient is diagnosed with recurrent AOM (“RAOM”). If middle ear effusion (“MEE”) persists in the middle ear for longer than three months, then the patient is diagnosed with chronic OME (“COME”).

AOM is very common and can affect both children and adults. AOM is usually a short-term inflammation of the middle ear, characterized by the sudden onset of one or more signs or symptoms of acute middle ear inflammation (e.g., ear pain, fever or irritability) in the presence of MEE. AOM is often preceded by upper respiratory symptoms including cough and rhinorrhea. Micro-organisms (viral or bacterial) in the nasopharynx may reflux into the middle ear, where they adhere and colonize resulting in an ear infection. AOM is extremely common in young children, many of whom will have multiple AOM episodes over the course of months or even years, resulting in a RAOM diagnosis.

OME is also very common and can affect both children and adults. OME is characterized by a non-purulent (non-infected) MEE without sudden onset of signs or symptoms of an acute ear infection. Symptoms usually involve conductive hearing loss or aural fullness caused by impaired transduction of sound waves through the fluid-filled middle ear, but typically without pain or fever. OME often follows an AOM episode and can last for several months or up to a year, which can result in speech and learning delays in children and other morbidities in both children and adults. There are several predisposing factors that have been associated with OME including environmental (e.g., bottle feeding, day-care setting, allergies to common environmental entities, cigarette smoke), age (higher incidence in pre-school age children), and ETD. Like AOM, patients can experience multiple OME episodes over the course of months or years, resulting in a diagnosis of recurrent OME (“ROME”). If MEE persists for longer than three months, then the patient is diagnosed with COME and is often considered as a surgical candidate to insert tympanostomy tubes to facilitate ventilating the middle ear.

An important component of middle ear health is a normally functioning ET. The ET is a small cilia-lined passageway that connects the middle ear to the back of the nasal cavity (nasopharynx). Its primary functions are to protect, drain, and ventilate the middle ear. Normally, it is collapsed, preventing material from entering the middle ear. The ET opens periodically upon swallowing, chewing, yawning, or when a pressure differential exists between the middle ear and the external environment. When the ET becomes blocked or does not open normally, ETD occurs.

Pathophysiology of Otitis Media:



The pathophysiology of OM and ETD are closely related. Both conditions can arise as a result of upper respiratory tract infections, allergies, and other inflammatory mediators and one condition can perpetuate the other condition. There are more than 700 million cases of OM and ETD around the world every year, half of which occur in children under five years of age. In the United States alone, there were more than 15 million visits to physicians during 2014 related to OM and ETD. It is one of the most common diseases seen in Pediatric and Otolaryngology practices and is the most frequent reason children consume antibiotics or undergo surgery.

To date, no drug product has been approved to treat OM. Antibiotics are commonly used to treat AOM patients who present with signs and symptoms of infection, but antibiotics have no effect on viral infections or OME which is a non-infectious condition. Topical steroids, antihistamines, and decongestants have not been shown to be effective as OM treatments or to prevent OM. In addition, the American Academy of Otolaryngology—Head and Neck Surgery recommends against use of these drugs in patients with OM. A commonly utilized option to treat and possibly prevent RAOM, ROME or COME, is to perform a surgery where the tympanic membrane is perforated to improve drainage and ventilation of the middle ear (myringotomy or tympanostomy tube insertions). However, surgery is not always an effective solution for all patients as many continue to suffer from OM or its complications, and sometimes require repeat surgeries. Managing recurrent and chronic OM drives billions of dollars in healthcare costs and results in millions of surgical procedures in children and adults around the world. There is a clear unmet need for a safe, non-antibiotic, non-surgical option for patients.

In 2016, the FDA permitted marketing of a medical device that uses a small intranasal balloon inserted into the ET to treat persistent ETD in adults. However, like OM, no drug product has been approved for the prevention of ETD.

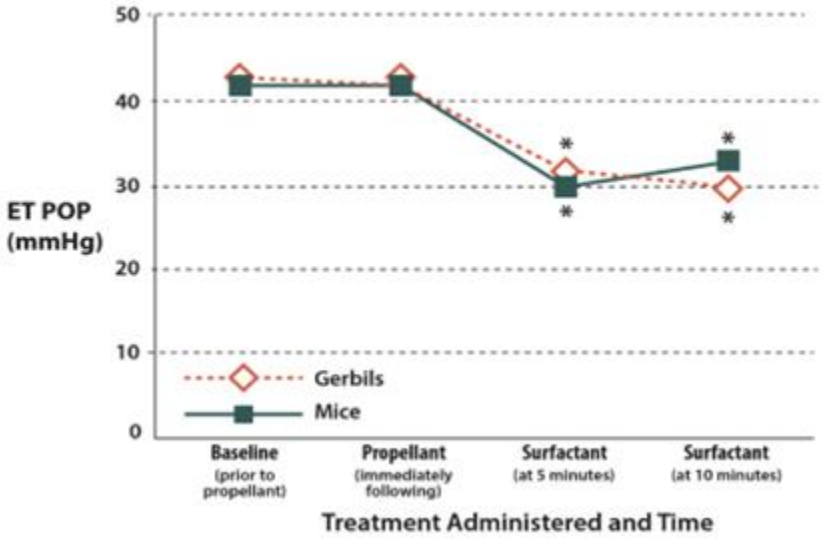
OP0201 nasal aerosol is a combination drug product candidate, comprised of a novel formulation of two surfactant active ingredients, DPPC and CP, and formulated with a propellant for easy administration. OP0201 is delivered as a local treatment through each nostril using a pMDI device. Together DPPC and CP are designed to effectively absorb to the air-liquid interface of the mucosa and reduce the interfacial surface tension of the ET, which reduces the passive pressure required for the ET to open. In other words, OP0201 is intended to promote ‘de-sticking’ of the ET so that ventilation of the middle ear may occur.

Avanti Polar Lipids, Inc. is our sole supplier of DPPC and CP, the active pharmaceutical ingredients used in OP0201 . Other manufacturers of DPPC and CP exist, but we have not yet qualified a secondary supplier. OP0201 nasal aerosol drug product candidate is currently manufactured using Good Manufacturing Practices by Sciarra Aeromed, Inc. We have not yet qualified a secondary manufacturer.

Surfactants are ubiquitous and well-understood endogenous compounds present in human nasal passages, the ET, and lung tissues, as well as in human milk and amniotic fluid. Surfactants have been evaluated under the hypothesis that exogenous administration of surfactant to a mucosal lined lumen such as the alveoli would result in de-sticking of the tissue and allowance of oxygen exchange in the lungs. In the case of the ET, it is known that the quantity of surfactants along the ET of children with OM is significantly reduced when compared to otologically healthy children. Also, the ET surface tension in patients with OM is higher than reported for patients with healthy ETs, causing the luminal surfaces to stick together. Indeed, reduction in ET luminal surface tension and passive opening pressure (“POP”), as well as improved ET function was demonstrated in a study of six cynomolgus monkeys who received injections of the calf lung surfactant extract INFASURF® (whose main component is the surfactant DPPC) directly into the ET lumen.

The positive effects of surfactants on ET function have been observed in preclinical animal studies using an early formulation of a DPPC and CP combination surfactant product. Meaningful reductions in POP of healthy ET, as well as meaningful reduction in severity and duration of OM episodes in three animal species after treatment were observed. In two separate animal-model experiments, the investigators studied the effects of intranasal administration of the early formulation on ET POP of the left ear as compared to propellant in healthy Mongolian gerbils and albino mice. In both animal species, administration of the product resulted in significant ($p<0.001$) reductions in mean ET POP measurements at both the 5 and 10-minute assessment times compared to baseline and immediately following propellant alone administration (Figures 1, 2 and 3). Among the gerbils, the mean (standard error [SE]) ET POP values (in millimeters of mercury [mmHg]) were 42.8 (2.29) at baseline, 42.43 (2.36) after propellant, 31.76 (1.74) at 5 minutes after surfactant, and 29.3 (1.51) at 10 minutes after surfactant. Similar findings were noted in the mice: mean (SE) ET POP values were 42.02 (1.22) at baseline, 42.02 (1.22) after propellant, 29.77 (1.69) at 5 minutes after surfactant, and 32.79 (1.77) at 10 minutes after surfactant.

Figure 1: Mean Passive Opening Pressures in Gerbil and Mice at Baseline, Immediately after Propellant, and at 5 and 10 Minutes after Surfactant Administration (Experiment 1)



* $p<0.05$ for surfactant treatment (each timepoint and animal group) compared to baseline and following propellant administration.

In a study of experimentally induced AOM in chinchillas, the use of the early formulation was associated with a marked reduction in the severity and duration of AOM. Furthermore, quantitative cultures of middle ear fluid showed dramatic decreases in bacterial colonization with intranasal treatment alone (i.e., no antibiotics were administered in this study). Based on these findings, Novus believes that resolution of MEE may occur significantly earlier with treatment. The data suggest that restoration of ET function and ventilation of the middle ear is beneficial in resolving bacterial AOM.

Prior to licensing rights to the surfactant program to Novus, the inventors treated nine humans who had various OM and ETD conditions. This human experience was captured as case studies and reported to the FDA. Based on these case studies, in conjunction with the preclinical animal data, Novus believes that a product candidate of this type may have utility in the treatment and prevention of OM and ETD in children and adults. Novus has completed three phase 1 clinical trials (studies C-001, C-002, C-004) of OP0201. Novus is currently conducting an exploratory phase 2a study in children with acute otitis media (study C-006).

- Study OP0201-C-001 (“C-001”) was a phase 1 clinical trial designed to evaluate safety, tolerability, and ET function following a single intranasal dose of OP0201 in 16 healthy adults. The randomized, double-blind, placebo-controlled, cross-over trial will explore the effect of a 20 mg dose of OP0201 on ET function. Assessment of ET function was captured using continuous tympanic impedance while subjects were exposed to changes in atmospheric pressure produced in a hyperbaric/hypobaric chamber. The single center study was conducted in Germany. Additional information about the study can be found at clinicaltrials.gov using the identifier NCT03828149.
- Study OP0201-C-002 (“C-002”) was a phase 1 clinical trial designed to evaluate safety and tolerability of daily intranasal administration of OP0201 over 14 consecutive days in 30 healthy adults. The randomized, double-blind, placebo-controlled, parallel-group, dose-escalation trial included a 30 mg per day dose (Cohort A) and 60 mg per day dose (Cohort B) of OP0201. The study was being conducted at a single phase 1 unit in the United States Additional information about the study can be found at clinicaltrials.gov using the identifier NCT03748758.
- Study OP0201-C-004 (“C-004”) was a phase 1 clinical trial designed to evaluate safety, tolerability, and relief of ear pain over a 60-minute observation period following a single intranasal dose of OP0201 in 24 adults with acute otitis media. The randomized, double-blind, placebo-controlled, parallel-group trial explored the effects of a 20 mg intranasal dose of OP0201. Assessment of pain relief was captured utilizing a Visual Analog Scale (“VAS”), Numeric Rating Scale (“NRS-11”), Patient Global Impression of Change (“PGIC”), and Clinical Global Impressions Scale: Global Improvement (“CGI-I”). The multicenter study was conducted in the United States Additional information about the study can be found at clinicaltrials.gov using the identifier NCT03766373.

- Study OP0201-C-006 (“C-006”) is an exploratory phase 2a clinical trial designed to evaluate safety, tolerability, and efficacy of daily intranasal administration of OP0201 over 10 consecutive days in approximately 100 pediatric patients, 6 to 24 months of age, with acute otitis media. The randomized, double-blind, placebo-controlled, parallel-group trial will explore the effects of a 20 mg per day dose of OP0201 as an adjunct to oral antibiotics. Patients will receive 10 days of treatment and will be followed for up to 30 days, during which multiple endpoints will be explored. The single center study will be conducted in the United States. Additional information about the study can be found at clinicaltrials.gov using the identifier NCT03818815.

Novus’ surfactant development program, if successful, will lead to registration of a surfactant-based product in North America and key European markets to treat and/or prevent OM in infants and children. Additional development activities to support registration in other countries, or for other indications, or other patient populations, may occur in the future.

Acute Otitis Externa (“AOE”)

AOE (or “swimmer’s ear”) is a generalized inflammation of the epithelium of the external ear canal that may also involve the pinna and/or the tympanic membrane (eardrum). The vast majority of AOE cases are due to bacterial infections, with *Pseudomonas aeruginosa* and *Staphylococcus aureus* being the most common pathogens. The condition is commonly associated with pain and characterized by redness of the ear canal (erythema), swelling of the tissue (edema), increased secretion of fluid, and shedding or peeling of the skin (desquamation of the epithelium). AOE occurs in all age groups and is more frequently observed in the summer months as well as in hot and humid environments. The most common treatment for AOE is antibiotics, with or without steroids, analgesics and avoiding ears being immersed underwater (e.g., swimming). Ear treatments are generally supplied in the form of liquids with several drops administered into each infected ear multiple times per day for a week or longer. In the United States alone, more than 5 million prescriptions for ear anti-infective products are prescribed every year, mostly for the treatment of AOE.

The current market leader in the ear anti-infective market is CIPRODEX®, marketed by Alcon, which according to IMS Health generated over $400 million in sales in the United States in 2015. It is a liquid suspension containing the antibiotic ciprofloxacin and the steroid dexamethasone. It is administered as four drops per infected ear, twice-daily over seven days for a total of 14 doses (56 drops placed into the ear canal over the course of a week). There are numerous other branded and generic ear anti-infectives, but none of these are clinically differentiated from CIPRODEX. Although effective when administered properly, liquid drops like these anti-infectives can be a challenge to administer into the ear, particularly in children. Proper administration requires the patient to lie down with the infected ear pointed upward, careful placement of multiple drops into the infected ear, manipulation of the ear lobe to move the liquid down into the ear canal, and the patient should remain still with the infected ear pointed upwards after applying the product for a period of time to prevent the medication from draining out of the ear. In addition, rapid resolution of otalgia (ear pain) is not achieved with any of the currently approved anti-infective products, even those that also contain an anti-inflammatory (e.g., steroid) in the formulation, like CIPRODEX.

Foam formulations such as OP0101 and OP0102 are becoming a prominent delivery system for topical drugs due to the intrinsic advantages of the platform: easy and fast administration, visibility of product during and after the administration, and complete coverage of large and variable surface areas as the product expands and molds to the shape of the cavity. In addition, foam formulations can remain in place for longer periods of time, increasing residence time of drugs at target sites. Finally, foam-based ear products can be administered while the patient is standing or sitting and do not require holding the head in any special orientation for a period of time.

Novus conducted four clinical trials of its first generation, antibiotic only formulation (OP0101), which it believes supported the utility of the foam platform in AOE. Data from the most recent clinical trial was announced in January 2015. The study was a 220 patient, phase 2, randomized, multicenter, parallel, active comparator trial in 220 AOE patients ages six months and older. During this trial, OP0101, which contains 0.3% ciprofloxacin, was administered once-daily for 7 days (7 doses) while the active comparator (CIPRODEX), which contains 0.3% ciprofloxacin and 0.1% dexamethasone, was administered twice-daily for 7 days (14 doses). The primary endpoint of the study was clinical cure, defined as score = 0 for erythema, edema, tenderness, ear discharge (otorrhea), and no further antibiotic required. Safety and efficacy of OP0101 was found to be non-inferior to CIPRODEX, even though OP0101 contained no steroid and utilized 50% fewer doses over the week-long course of therapy. Although OP0101 proved to be effective in treating AOE infection, the product candidate is not sufficiently differentiated from other products in the market. Novus believes that none of the currently marketed products adequately address the greatest unmet need, which is rapid pain relief. Therefore, in 2016, Novus began development of OP0102, a second-generation formulation designed to rapidly relieve ear pain and eradicate infection with less than seven days of treatment. Novus subsequently paused OP0102 development to focus resources on the surfactant program.

The competitive conditions faced by the Company are described in greater detail in Part I, Item 1A. *Risk Factors* in this Annual Report on Form 10-K under the caption "We face substantial competition, which may result in others discovering, developing or commercializing competing products before or more successfully than we do."

Intellectual Property

Novus' success depends in part on its ability to obtain and maintain proprietary protection for its product candidates, novel discoveries, product technologies and other know-how, to operate without infringing on the proprietary rights of others and to prevent others from infringing Novus' proprietary rights. Novus seeks to protect its product candidates by, among other methods, filing U.S. and foreign patent applications related to its proprietary technology, inventions and improvements that are important to the development and implementation of its business. Novus also relies on trademarks, trade secrets, know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain Novus' proprietary protection for Novus' product candidates.

Novus' intellectual property portfolio includes issued patents and patent applications directed towards products derived from Novus' surfactant platform and foam platform with claims to drug substance, pharmaceutical preparations as well as to methods of treatment. For OP0201, Novus owns or has exclusive rights to one U.S. patent application, one international application, and seven foreign patent applications. If allowed. the last to expire patent application will expire in December 2039, absent any adjustments or extensions. For OP0101 and OP0102, Novus owns or has exclusive rights to two families of patents, one with three United States and seven foreign patents (Canada, France, Germany, Israel, Italy, Spain, and the United Kingdom), and a second with two United States and five foreign patents (France, Germany, Italy, Spain and the United Kingdom). In the first family the last to expire issued patent in the United States will expire in September 2027, including patent term adjustment. In the second family the last to expire issued patent in the United States will expire in December 2033.

Patents extend for varying periods according to the date of patent filing or grant and the legal term of patents in various countries where patent protection is obtained. The actual protection afforded by a patent, which can vary from country to country, depends on the type of patent, the scope of its coverage and the availability of legal remedies in the country.

Novus also protects its proprietary information by requiring its employees, consultants, contractors and other advisors to execute nondisclosure and assignment of invention agreements upon commencement of their respective employment or engagement. In addition, Novus also requires confidentiality or service agreements from third parties that receive confidential information or materials.

License Agreement with Otodyne, Inc.

In November 2015, Novus entered into a license agreement with Scientific Development and Research, Inc. and Otodyne, Inc. granting Novus exclusive worldwide rights to develop and commercialize surfactant-based products. Under the terms of the agreement, Novus is obligated to use commercially reasonable efforts to seek approval for and commercialize at least one product for OM in the United States and key European markets (France, Germany, Italy, Spain, and the United Kingdom). Novus is responsible for prosecuting, maintaining, and enforcing all intellectual property and will be the sole owner of improvements.

In December 2015, Otodyne completed transfer of all technology, including the active investigational new drug application ("IND"), to Novus. Novus is obligated to pay up to $42.1 million in development and regulatory milestones if OP0201 is approved for three indications in the United States, two in Europe, and two in Japan. Novus is also obligated to pay up to $36.0 million in sales-based milestones, beginning with sales exceeding $1.0 billion in a calendar year. Novus is also obligated to pay a tiered royalty for a period up to eight years, on a country-by-country basis. The royalty ranges from low-single to mid-single percent of net sales. The Company made a $300,000 milestone payment in March 2019 related to the first patient enrolled in a phase 2 study. There were no other milestones achieved during the years ended December 31, 2019 or 2018.

Government Regulation

Government authorities in the United States, including federal, state, and local authorities, and in other countries, extensively regulate, among other things, the manufacturing, research and clinical development, marketing, labeling and packaging, storage, distribution, post-approval monitoring and reporting, advertising and promotion, and export and import of pharmaceutical and biological products, such as those we are developing. Pricing of such products is also subject to regulation in many countries. 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.

U.S. Government Regulation

The FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA") and its implementing regulations, and biologics under the FDCA and the Public Health Service Act ("PHSA") and its implementing regulations. FDA approval is required before any new unapproved drug or biologic or dosage form, including a new use of a previously approved drug, can be marketed in the U.S. Drugs and biologics are also subject to other federal, state, and local statutes and regulations. If we fail to comply with applicable FDA or other requirements at any time during the product development process, clinical testing, approval process or after approval, we may become subject to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, untitled or warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. Any FDA enforcement action could have a material adverse effect on us.

The process required by the FDA before product candidates may be marketed in the United States generally involves the following:

- completion of extensive preclinical laboratory tests and preclinical animal studies, all performed in accordance with the Good Laboratory Practices ("GLP") regulations;
- submission to the FDA of an IND which must become effective before human clinical trials may begin and must be updated annually;
- approval by an independent institutional review board ("IRB") or ethics committee representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the product candidate for each proposed indication;
- completion of manufacturing scale up and stability studies, all performed in accordance with the Good Manufacturing Practices "GMP" regulations;
- preparation of and submission to the FDA of a biologics license application ("BLA") or a new drug application, or NDA, after completion of all pivotal clinical trials;
- potential review of the product application by an FDA advisory committee, where appropriate and if applicable;
- a determination by the FDA within 60 days of its receipt of a BLA or NDA to file the application for review;
- satisfactory completion of a FDA pre-approval inspection of the manufacturing facilities where the proposed product is produced to assess compliance with current Good Manufacturing Practices ("cGMP") regulations;
- potential FDA audit of the clinical trial sites that generated the data in support of the BLA or NDA; and
- FDA review and approval of a BLA or NDA prior to any commercial marketing or sale of the product.

The preclinical and clinical 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.

An IND is a request for authorization from the FDA to administer an investigational new drug product to humans in clinical trials. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human trials. 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 new drug. An IND must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to the proposed clinical trials. 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 clinical trials can begin. Accordingly, submission of an IND may or may not result in the FDA allowing clinical trials to commence. The FDA may impose a clinical hold at any time during clinical trials and may impose a partial clinical hold that would limit trials, for example, to certain doses or for a certain length of time.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with Good Clinical Practices ("GCPs") which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. 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 efficacy criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. Additionally, approval must also be obtained from each clinical trial site's IRB before the trials may be initiated, and the IRB must monitor the trial until completed. There are also requirements governing the reporting of ongoing clinical trials and clinical trial results to public registries.

The clinical investigation of a drug is generally divided into three phases. Although the phases are usually conducted sequentially, they may overlap or be combined.

- Phase 1. The drug is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to evaluate the safety, dosage tolerance, metabolism and pharmacologic actions of the investigational new drug in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness.
- Phase 2. The drug is administered to a limited patient population to evaluate dosage tolerance and optimal dosage, identify possible adverse side effects and safety risks, and preliminarily evaluate efficacy.
- Phase 3. The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites to generate enough data to evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the investigational new drug product, and to provide an adequate basis for physician labeling.

In some cases, the FDA may condition approval of a BLA or NDA for a product candidate on the sponsor's agreement to conduct additional clinical trials after approval. In other cases, a sponsor may voluntarily conduct additional clinical trials after approval to gain more information about the drug. Such post-approval studies are typically referred to as Phase 4 clinical trials.

Sponsors must also report to the FDA, within certain timeframes, serious and unexpected adverse reactions, any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator's brochure, or any findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the product candidate. The FDA, the IRB, or the clinical trial sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial. We may also suspend or terminate a clinical trial based on evolving business objectives or competitive climate.

The clinical trial process can take three to ten years or more to complete, and there can be no assurance that the data collected will support FDA approval or licensure of the product. Results from one trial are not necessarily predictive of results from later trials.

A drug being studied in clinical trials may be made available to individual patients in certain circumstances. Pursuant to the 21st Century Cures Act ("Cures Act") which was signed into law in December 2016, the manufacturer of an investigational drug for a serious disease or condition is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for individual patient access to such investigational drug (compassionate use). This requirement applies on the later of 60 calendar days after the date of enactment of the Cures Act or the first initiation of a Phase 2 or Phase 3 trial of the investigational drug. At this time, Novus does not have a program for the compassionate use of an investigational product outside of a clinical trial as it is not applicable to our investigational products.

Submission of a BLA or NDA to the FDA

Assuming successful completion of all required testing (e.g. completion of pivotal clinical trials) in accordance with all applicable regulatory requirements, detailed investigational new drug product information is submitted to the FDA in the form of a BLA or NDA requesting approval to market the product for one or more indications. Under federal law, the submission of most BLAs and NDAs is subject to an application user fee and these fees are typically increased on an annual basis. Applications for orphan drug products are exempted from the BLA and NDA user fees and may be exempted from product and establishment user fees, unless the application includes an indication for other than a rare disease or condition. No application user fees are anticipated for OP0201 in calendar 2020.

A BLA or NDA for a new molecular entity must include all relevant data available from pertinent preclinical studies and clinical trials, 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 trials intended to test the safety and effectiveness of a use of a product, or from several alternative sources, including investigator-initiated trials that are not sponsored by Novus. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational new drug product to the satisfaction of the FDA.

Once a BLA or NDA for a new molecular entity has been submitted, 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 the FDA's requests for additional information or clarification.

Before approving a BLA or NDA, the FDA typically will 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 a BLA or NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

The FDA's Decision on a BLA or NDA

The FDA evaluates a BLA to determine whether the data demonstrate that the biologic is safe, pure, and potent, or effective, and an NDA to determine whether the drug is safe and effective. After the FDA evaluates the BLA or NDA and conducts inspections of manufacturing facilities where the product will be produced, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug 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 require additional clinical data or an additional pivotal Phase 3 clinical trial(s), or other significant, expensive and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. Even if such additional information is submitted, the FDA may ultimately decide that the BLA or NDA does not satisfy the criteria for approval and issue a denial. The FDA could also approve the BLA or NDA with a Risk Evaluation and Mitigation Strategy ("REMS") plan 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, development of adequate controls and specifications, or a commitment to conduct one or more post-market studies or clinical trials. Such post-market testing may include Phase 4 clinical trials and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

Drug manufacturers are subject to periodic unannounced inspections by the FDA and state agencies for compliance with cGMP requirements. 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 and documentation 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 rely, and expect to continue to rely, on third parties for the production of clinical quantities of our product candidates and expect to rely in the future on third parties for the production of commercial quantities. Future FDA and state inspections may identify compliance issues at our facilities or at the facilities of our contract manufacturers that may disrupt production, 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 BLA or 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. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution 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, untitled or warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending BLAs or NDAs or supplements to approved BLAs or NDAs, or suspension or revocation of licenses or withdrawal of 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 strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications 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, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Orphan Designation and Exclusivity

The FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making the drug for this type of disease or condition will be recovered from sales in the United States.

Orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. In addition, if a product is the first to receive FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity.

Pediatric Trials and Exclusivity

Under the Pediatric Research Equity Act of 2003 ("PREA") as amended, BLAs and NDAs must contain data to assess the safety and effectiveness of an investigational new drug product for the claimed indications in all relevant pediatric populations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. A sponsor who is planning to submit a marketing application for a drug product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration must submit an initial Pediatric Study Plan ("PSP") within sixty days of an end-of-phase 2 meeting or as may be agreed between the sponsor and the FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults or full or partial waivers if certain criteria are met. The FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials, and/or other clinical development programs. The requirements for pediatric data do not apply to any drug for an indication for which orphan designation has been granted.

Pediatric exclusivity is another type of non-patent exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the five-year and three-year non-patent and orphan exclusivity. This six-month exclusivity may be granted if a BLA or NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of FDA-requested pediatric trials are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection covering the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot accept or approve another application relying on the BLA or NDA sponsor's data.

Patent Term Restoration

Depending upon the timing, duration, and specifics of the FDA approval of the use of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a BLA or NDA, plus the time between the submission date and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent and within 60 days of the product's approval. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of the patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant BLA or NDA.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application ("ANDA") to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug ("RLD").

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to an RLD if "the rate and extent of absorption of the generic drug do not show a significant difference from the rate and extent of absorption of the listed drug..."

Upon approval of an ANDA, the FDA indicates that the generic product is "therapeutically equivalent" to the RLD and it assigns a therapeutic equivalence rating to the approved generic drug in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider an "AB" therapeutic equivalence rating to mean that a generic drug is fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of an "AB" rating often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

The FDCA provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity. In cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or a method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA applicant.

European Union/Rest of World Government Regulation

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. The cost of establishing a regulatory compliance system for numerous varying jurisdictions can be very significant. Although many of the issues discussed above with respect to the United States apply similarly in the context of the European Union ("EU") and in other jurisdictions, the approval process varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Whether or not we obtain FDA approval for a product candidate, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In the EU, for example, a clinical trial authorization application ("CTA") must be submitted for each clinical protocol to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is accepted in accordance with a country's requirements, the clinical trial may proceed.

The requirements and process governing the conduct of clinical trials vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP the applicable regulatory requirements, and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational medicinal product under EU regulatory systems, we must submit a marketing authorization application. The content of the BLA or NDA filed in the United States is like that required in the EU, except, among other things, country-specific document requirements

For other countries outside of the EU, such as countries in Eastern Europe, Latin America or Asia, the requirements governing product licensing, pricing, and reimbursement vary from country to country.

Countries that are part of the EU, as well as countries outside of the European Union, have their own governing bodies, requirements, and processes with respect to the approval of pharmaceutical and biologic products. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Authorization Procedures in the EU

Medicines can be authorized in the EU by using either the centralized authorization procedure or national authorization procedures.

- Centralized procedure. The EMA implemented the centralized procedure for the approval of human medicines to facilitate marketing authorizations that are valid throughout the European Economic Area ("EEA"). This procedure results in a single marketing authorization issued by the EMA that is valid across the EEA. The centralized procedure is compulsory for human medicines that are: derived from biotechnology processes, such as genetic engineering, contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions, and officially designated orphan medicines.
- For medicines that do not fall within these categories, an applicant has the option of submitting an application for a centralized marketing authorization to the European Commission following a favorable opinion by the EMA, as long as the medicine concerned is a significant therapeutic, scientific or technical innovation, or if its authorization would be in the interest of public health.
- National authorization procedures. There are also two other possible routes to authorize medicinal products in several EU countries, which are available for investigational medicinal products that fall outside the scope of the centralized procedure:
- Decentralized procedure. Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one EU country of medicinal products that have not yet been authorized in any EU country and that do not fall within the mandatory scope of the centralized procedure.
- Mutual recognition procedure. In the mutual recognition procedure, a medicine is first authorized in one EU Member State, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other EU countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

In some cases, a Pediatric Investigation Plan ("PIP") or a request for waiver or deferral, is required for submission prior to submitting a marketing authorization application. A PIP describes, among other things, proposed pediatric trials and their timing relative to clinical trials in adults. Because Novus intends to pursue pediatric indications for OP0201 before adult indications, a PIP will be submitted to EMA and other EU countries, as required. The PIP will need to be submitted early during product development, before marketing authorization applications are submitted. The timing of PIP submission cannot be after initiation of pivotal trials or confirmatory (phase 3) trials.

Exclusivity of New Chemical Entities and New Fixed Dose Combinations

In the EU, new chemical entities, sometimes referred to as new active substances as well as new fixed dose combinations, qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic (abbreviated) application for eight years, after which a generic application can be submitted, and the innovator's data may be referenced, but not approved for two years. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

Exceptional Circumstances/Conditional Approval

Orphan drugs or drugs with unmet medical needs may be eligible for EU approval under exceptional circumstances or with conditional approval. Approval under exceptional circumstances may be applicable to orphan products and is used when an applicant is unable to provide comprehensive data on the efficacy and safety under normal conditions of use because the indication for which the product is intended is encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence, when the present state of scientific knowledge does not allow comprehensive information to be provided, or when it is medically unethical to collect such information. Conditional marketing authorization may be applicable to orphan medicinal products, medicinal products for seriously debilitating or life-threatening diseases, or medicinal products to be used in emergency situations in response to recognized public threats. Conditional marketing authorization can be granted on the basis of less complete data than is normally required in order to meet unmet medical needs and in the interest of public health, provided the risk-benefit balance is positive, it is likely that the applicant will be able to provide the comprehensive clinical data, and unmet medical needs will be fulfilled. Conditional marketing authorization is subject to certain specific obligations to be reviewed annually.

Accelerated Review

Under the centralized procedure in the EU, the maximum timeframe for the evaluation of a marketing authorization application is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the EMA's Committee for Medicinal Products for Human Use, or CHMP). Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. In this circumstance, EMA ensures that the opinion of the CHMP is given within 150 days, excluding clock stops.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we obtain regulatory approval. In the United States and in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of coverage and reimbursement from third-party payors. Third-party payors include government authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. Moreover, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third- party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain regulatory approvals. Our product candidates may not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit.

The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. By way of example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively, the Affordable Care Act, contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal healthcare programs. Some of the provisions of the Affordable Care Act have yet to be fully implemented, while certain provisions have been subject to judicial and congressional challenges. In January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, that while not a law, is widely viewed as the first step toward the passage of legislation that would repeal certain aspects of the Affordable Care Act. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Congress also could consider subsequent legislation to replace elements of the Affordable Care Act that are repealed. Thus, the full impact of the Affordable Care Act, any law replacing elements of it, or the political uncertainty surrounding its repeal or replacement on our business remains unclear. Adoption of government controls, measures and tightening of restrictive policies in jurisdictions with existing controls and measures could limit payments for pharmaceuticals.

In European countries, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines but monitor and control company profits. The downward pressure on healthcare costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, the emphasis on cost containment measures in the United States and other countries has increased, and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Other Healthcare Laws and Compliance Requirements

If we obtain regulatory approval for any of our product candidates, we may be subject to various federal and state laws targeting fraud and abuse in the healthcare industry. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;
- the federal Health Insurance Portability and Accountability Act of 1996, ("HIPAA"), which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- the federal transparency laws, including the provision of the Affordable Care Act referred to as the federal Physician Payment Sunshine Act, that requires drug and biologics manufacturers to disclose payments and other transfers of value provided to physicians and teaching hospitals and ownership interests of physicians and their immediate family members;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act ("HITECH") and its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information; and
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws that may apply to items or services reimbursed by any third-party payor, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

The Affordable Care Act broadened the reach of the fraud and abuse laws by, among other things, amending the intent requirement of the federal Anti-Kickback Statute and the applicable criminal healthcare fraud statutes contained within 42 U.S.C. § 1320a-7b. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the Affordable Care Act provides that 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 civil False Claims Act or the civil monetary penalties statute. Many states have adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs.

We are also subject to the U.S. Foreign Corrupt Practices Act ("FCPA") which prohibits improper payments or offers of payments to foreign governments and their officials for the purpose of obtaining or retaining business. Safeguards we implement to discourage improper payments or offers of payments by our employees, consultants, and others may be ineffective, and violations of the FCPA and similar laws may result in severe criminal or civil sanctions, or other liabilities or proceedings against us, any of which would likely harm our reputation, business, financial condition and result of operations.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, exclusion from participation in government healthcare programs, such as Medicare and Medicaid and imprisonment, damages, fines and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Employees

As of March 22, 2020, Novus had eight employees, seven of which were full-time employees. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Corporate Information

Otic Pharma, Ltd. ("Otic") was founded in the State of Israel in 2008. In 2015, Otic established U.S. operations and moved its corporate headquarters to Irvine, California. In 2017, Otic consummated a reverse merger with Tokai Pharmaceuticals, Inc. ("Tokai"), a Delaware corporation that was incorporated on March 26, 2004, pursuant to which, among other things, Tokai purchased from Otic and its stockholders all of the common and preferred shares of Otic in exchange for the issuance of a certain number of shares of common stock of Tokai (the "Reverse Merger"). Following the Reverse Merger, Tokai changed its name to Novus Therapeutics, Inc. Our executive offices are located at 19900 MacArthur Boulevard, Suite 550, Irvine, California 92612. Our telephone number is (949) 238-8090 and our website is novustherapeutics.com. We do not incorporate the information on or accessible through our website into this Annual Report, and you should not consider any information on, or that can be accessed through, our website as part of this Annual Report on Form 10-K.

You are advised to read this Annual Report on Form 10-K in conjunction with other reports and documents that we file from time to time with the Securities and Exchange Commission ("SEC"). In particular, please read our definitive proxy statement, which will be filed with the SEC in connection with our 2020 annual meeting of stockholders, our quarterly reports on Form 10-Q and any current reports on Form 8-K that we may file from time to time. You may obtain copies of these reports after the date of this annual report directly from us or from the SEC at its website at www.sec.gov. We make our periodic and current reports available on our internet website, free of charge, as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC.

Item 1A. Risk Factors.

An investment in shares of our common stock involves a high degree of risk. You should carefully consider the following risk factors, as well as the other information in this Annual Report on Form 10-K, and in our other public filings. The occurrence of any of these risks could harm our business, financial condition, results of operations and/or growth prospects or cause our actual results to differ materially from those contained in forward-looking statements we have made in this report and those we may make from time to time. You should consider all of the risk factors described in our public filings when evaluating our business.

Risks Related to Our Operations

We have incurred significant operating losses since our inception and expect that we will continue to incur losses over the next several years and may never achieve or maintain profitability.

We have incurred significant annual net operating losses in every year since our inception. We have no products approved for commercial sale and have not generated any revenue from product sales to date, and we continue to incur significant research and development and other expenses related to our ongoing operations. If OP0201 or any future product candidates we develop are not successfully developed and approved, we may never generate any revenue from sales of products. The Company has experienced net losses and negative cash flows from operating activities since its inception. The Company's net loss for the year ended December 31, 2019 is $16.0 million and the Company has an accumulated deficit of $57.6 million. We have not generated any revenues from product sales, have not completed the development of any product candidate and may never have a product candidate approved for commercialization. We expect it will be several years, if ever, before we have a product candidate ready for commercialization. We have financed our operations to date primarily through sales of equity. We have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and our clinical trials. Our net losses may fluctuate significantly from quarter to quarter and year to year and will depend, in part, on the rate at which we incur expenses and our ability to generate revenue. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital.

We are focused primarily on developing products from the surfactant platform as a potential first-in-class treatment option for patients at risk for or with OM (middle ear inflammation with or without infection). Although we have successfully manufactured cGMP batches of OP0201 nasal aerosol drug product suitable for our phase 1 and phase 2a clinical trials, this was done on a smaller scale with a drug product that has a short shelf life. Additional development of OP0201 and/or the dry-powder unit dose device product candidate will be required prior to initiation of future clinical trials. The full cost and timing of this additional development is uncertain, although we expect it will require at least 12-months of formulation development before a product candidate is selected. We expect that it will be several years, if ever, before we have a product candidate ready for commercialization. If we are unable to successfully generate clinical data for the surfactant program, we may have greater difficulty raising additional capital on favorable terms, or at all.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses that we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if, and as we:

- continue formulation development of our surfactant product candidates;
- continue device development for our drug-device product candidates;
- continue nonclinical and clinical development of our product candidates;
- seek to identify and acquire additional product candidates;
- acquire or in-license other products and technologies;
- enter into collaboration arrangements with regards to product discovery or development;
- develop manufacturing processes;
- seek marketing approvals for any of our product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;
- hire additional personnel;

- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and
- operate as a public company.

To become and remain profitable, we must develop and eventually commercialize a product or products with significant market potential. This will require us to be successful in a range of challenging activities, including completing clinical trials of our product candidates, obtaining marketing approval for these product candidates and manufacturing, marketing and selling those products for which we obtain marketing approval. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of the Company, could impair our ability to raise capital, maintain our nonclinical and clinical development efforts, and expand our business or continue our operations and may require us to raise additional capital that may dilute the ownership interest of common stockholders. A decline in the value of the Company could also cause stockholders to lose all or part of their investment.

We are early in our development efforts and currently have only one product candidate in clinical development. If we are unable to successfully develop and commercialize this or any other product candidate, or if we experience significant delays in doing so, our business will be materially harmed.

We currently do not have any products that have gained regulatory approval. We have invested substantially all our efforts and financial resources in product development, including funding our formulation and device development, manufacturing, nonclinical studies, and clinical trials. Our ability to generate product revenues, which we do not expect will occur for several years, if ever, will depend heavily on the successful development and eventual commercialization of one or more drug candidates. As a result, our business is substantially dependent on our ability to successfully complete the development of and obtain regulatory approval for our, or additional product candidates.

We 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 pharmaceutical area. For example, to execute our business plan, we will need to successfully:

- execute formulation, manufacturing, clinical, and nonclinical development activities;
- manufacture drug product at commercial scale;
- establish and confirm commercially acceptable stability (shelf-life) of our drug products;
- in-license or acquire other product candidates and advance them through clinical development;
- obtain required regulatory approvals for the development and commercialization of OP0201 or other product candidates;
- maintain, leverage and expand our intellectual property portfolio;
- build and maintain robust sales, distribution and marketing capabilities, either on our own or in collaboration with strategic partners;
- gain market acceptance for any approved and marketed drug products;
- obtain and maintain adequate product pricing and reimbursement;
- develop and maintain any strategic relationships we elect to enter; and
- manage our spending as costs and expenses increase due to product manufacturing, nonclinical development, clinical trials, regulatory approvals, post-marketing commitments, and commercialization.

If we are unsuccessful in accomplishing these objectives, we may not be able to successfully develop and commercialize our or other product candidates, and our business will suffer.

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

We are an early development stage pharmaceutical company. Our ongoing operations to date have been limited to organizing and staffing the Company, business planning, raising capital, acquiring and developing technology, identifying potential product candidates. Since then, operations related to development of OP0201 nasal aerosol have included arranging for third party vendors to formulate and manufacture cGMP clinical material as well as preparing and conducting three phase 1 clinical trials and one phase 2a clinical trial. We have not yet demonstrated our ability to successfully manufacture drug product in large enough quantities and with stability to support additional clinical trials, execute pivotal clinical trials, obtain marketing approvals, manufacture a commercial scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. It can take many years to develop a new medicine from the time it is discovered to when it is available for treating patients. Consequently, any predictions made about our future success or viability based on our short operating history to date may not be as accurate as they could be if we had a longer operating history.

In addition, as an early stage business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. To successfully market any of our product candidates, we will need to transition from a company with a clinical development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

Drug development involves a lengthy and expensive process with an uncertain outcome, including failure to demonstrate safety and efficacy to the satisfaction of the FDA or similar regulatory authorities outside the United States. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the formulation and commercialization of our product candidates.

We continue to conduct formulation and device development of products from the surfactant platform. We are highly dependent on third parties for formulation and device development as well as manufacturing of drug product for future clinical trials and commercial supply.

There is a risk that additional nonclinical and/or clinical safety studies will be required by the FDA or similar regulatory authorities outside the U.S. and/or that subsequent studies will not match results seen in prior studies.

Reformulation work for OP0102 foam otic to explore adding a second active ingredient (anesthetic) to address immediate relief of ear pain associated with AOE commenced in 2016 but was subsequently put on hold in 2017. If development of OP0102 foam otic is resumed, additional formulation development and clinical trials with the new foam otic combination product (antibiotic and anesthetic) will need to be conducted.

Given the early stage of development for both products, the risk of failure for both of our product candidates is high. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete formulation and device development for our products, conduct nonclinical trials, and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Formulation and device development, nonclinical and clinical testing are all expensive activities, difficult to design and implement, and can take years to complete. The outcome of nonclinical and clinical trials is inherently uncertain. Failure can occur at any time during the development program, including during the clinical trial process. Further, the results of nonclinical studies and early clinical trials of our product candidates, as well as earlier generation formulations may not be predictive of the results of later-stage clinical trials. Interim results of a clinical trial do not necessarily predict final results. For instance, the results of our studies with the earlier generation OP0101 formulation may not be predictive of the results of studies conducted with OP0102 formulation, if such program is resumed. Moreover, nonclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in nonclinical and clinical trials have nonetheless failed to obtain marketing approval of their products. It is impossible to predict when or if any of our product candidates will prove effective, safe and well-tolerated in humans or will receive regulatory approval.

We may experience delays in our clinical trials, and we do not know whether planned clinical trials will begin or enroll subjects on time, need to be redesigned or be completed on schedule, if at all. There can be no assurance that the EMA, or the Medicines & Healthcare Products Regulatory Agency ("MHRA"), the United Kingdom regulatory authority, will approve Clinical Trial Application's for any of our product candidates in the future. There is also no assurance that the FDA will not put any of our product candidates on clinical hold in the future. We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates. Clinical trials may be delayed, suspended or prematurely terminated for a variety of reasons, such as:

- delay or failure in reaching agreement with the FDA, EMA, MHRA or a comparable foreign regulatory authority on a trial design that we want to execute;
- delay or failure in obtaining authorization to commence a trial or inability to comply with conditions imposed by a regulatory authority regarding the scope or design of a clinical trial;
- delays in reaching, or failure to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- delays in completing formulation development and manufacturing as a prerequisite to commencing clinical work;
- inability, delay, or failure in identifying and maintaining a sufficient number of trial sites, many of which may already be engaged in other clinical programs;
- delay or failure in recruiting and enrolling suitable subjects to participate in a trial;
- delay or failure in having subjects complete a trial or return for post-treatment follow-up;
- clinical sites and investigators deviating from trial protocol, failing to conduct the trial in accordance with regulatory requirements, or dropping out of a trial, including the possibility we could learn of additional subjects who were exposed by predecessor IND sponsors to investigational drugs outside of clinical protocols;
- lack of adequate funding to continue the clinical trial, including the incurrence of unforeseen costs due to enrollment delays, requirements to conduct additional clinical trials and increased expenses associated with the services of our contract research organizations ("CROs") and other third parties;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, or participants may drop out of these clinical trials at a higher rate than we anticipate;
- we may experience delays or difficulties in the enrollment of patients that our product candidates are designed to target;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may have difficulty partnering with experienced CROs and study sites that can identify patients that our product candidates are designed to target and run our clinical trials effectively;
- regulators or IRBs may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; or
- there may be changes in governmental regulations or administrative actions. In addition, our development and commercialization activities could be harmed or delayed by a shutdown of the U.S. government, including the FDA. For example, a prolonged shutdown may significantly delay the FDA's ability to timely review and process any submissions we may file or cause other regulatory delays, which could materially and adversely affect our business.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive, or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings that would reduce the potential market for our products or inhibit our ability to successfully commercialize our products;
- be subject to additional post-marketing restrictions and/or testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in testing or marketing approvals. We do not know whether any of our nonclinical studies or clinical trials will need to be restructured or will be completed on schedule, or at all. Significant nonclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or may allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

Additionally, because we are developing a drug-device combination product, we will be subject to greater regulatory scrutiny and technical challenges. Devices such as our metered-dose inhaler are regulated by a separate division within the FDA. Even if our drug compound is shown to be safe and effective, our delivery device must also demonstrate that it can reliably deliver a consistent dose of the drug across repeated uses. This is challenging and is subject to a further layer of regulatory review before our product can be approved. If we are unsuccessful in addressing these technical and regulatory challenges, our prospects could be adversely affected.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented and expenses for the development of our product candidates could increase.

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials to demonstrate safety and efficacy. We do not know whether the ongoing or planned clinical trials will enroll subjects in a timely fashion, require redesign of essential trial elements or be completed on its projected schedule. In addition, competitors may have ongoing clinical trials for product candidates that treat related or the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether.

Patient enrollment is affected by other factors including:

- the eligibility criteria for the study in question;
- the perceived risks and benefits of the product candidate under study;
- the efforts to facilitate timely enrollment in clinical trials;
- the inability to identify and maintain a sufficient number of trial sites, many of which may already be engaged in other clinical trial programs, including some that may be for the same disease indication;
- the patient referral practices of physicians;
- the proximity and availability of clinical trial sites for prospective patients;
- the seasonality and severity of diseases that affect enrollment (e.g. influenzae season for OM);
- ambiguous or negative interim results of our clinical trials, or results that are inconsistent with earlier results;
- feedback from regulatory authorities, IRBs, ethics committees ("ECs"), or data safety monitoring boards, or results from earlier stage or concurrent nonclinical and clinical trials, that might require modifications to the protocol;

- decisions by regulatory authorities, IRBs, ECs, or the Company, or recommendations by data safety monitoring boards, to suspend or terminate clinical trials at any time for safety issues or for any other reason; and
- unacceptable risk-benefit profile or unforeseen safety issues or adverse effects.

Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of the Company to decline and limit our ability to obtain additional financing.

If serious adverse events or unacceptable side effects are identified during the development of our product candidates, we may need to abandon or limit our development of some of our product candidates.

If our product candidates are associated with undesirable effects in nonclinical or clinical trials or have characteristics that are unexpected, we may need to interrupt, delay or abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Any occurrences of clinically significant adverse events with our product candidates may harm our business, financial condition and prospects significantly.

OP0201 nasal aerosol is an early-product candidate, and the side effect profile in humans has not been fully established. Currently unknown, drug-related side effects may be identified through ongoing and future clinical trials and, as such, these possible drug-related side effects could affect patient recruitment, the ability of enrolled subjects to complete the trial, or result in potential product liability claims. The side effect profile of the dry-powder unit dose product candidate will need to be fully established and the safety profile may differ from the safety profile of OP0201 nasal aerosol.

Risks Related to Our Financial Position and Need for Additional Capital

We have concluded and disclosed in the footnotes to our consolidated financial statements, included elsewhere within this Annual Report, that we do not have sufficient cash to fund our operations through 12 months from the date of issuance of the most recent financial statements.

Our consolidated financial statements included in this Annual Report have been prepared on a basis that assumes that we will continue as a going concern and does not include any adjustments that may result from the outcome of this uncertainty.

Our ability to continue as a going concern is dependent upon a number of factors, including our ability to obtain the necessary financing to meet our obligations and repay our liabilities arising from obligations that become due in the ordinary course of business. Management currently believes that it will be necessary for us to raise additional funding in the form of an equity financing from the sale of common stock. There can be no guarantee that we will successfully raise all the funding we require. However, substantial doubt about a company's ability to continue as a going concern is generally viewed unfavorably by current and prospective investors, as well as by analysts and creditors. As a result, it may be more difficult for us to raise the additional financing necessary to continue to operate our business and we may be forced to significantly alter our business strategy, substantially curtail our current operations, or cease operations altogether.

We will need substantial additional funding. If we are unable to raise capital when needed, we would be compelled to delay, reduce or eliminate our product development programs orexplore strategic alternatives resulting in a merger or sale of the company.

We expect our expenses to increase in parallel with our ongoing activities, particularly as we continue our nonclinical and clinical development, identify new clinical candidates and initiate clinical trials of, and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our nonclinical and clinical development programs or any future commercialization efforts.

We have sufficient capital to complete the ongoing OP0201 phase 2a clinical trial but will require additional capital to conduct additional surfactant formulation and manufacturing activities, additional clinical trials and ultimately to commercialize a surfactant drug product, if approved. We may also need to raise additional funds to pursue other development activities related to additional product candidates that we may develop. Our funding needs may fluctuate significantly based on a number of factors, such as:

- the scope, progress, results and costs of formulation development and manufacture of drug product to support nonclinical and clinical development of our product candidates;
- the extent to which we enter into additional collaboration arrangements regarding product discovery or development, or acquire or in-license products or technologies;
- our ability to establish additional collaborations with favorable terms, if at all;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of future commercialization activities, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval; and
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims.

Identifying potential product candidates and conducting formulation development, nonclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Even if we generate positive clinical data, additional financing may not be available to us on acceptable terms, or at all. If we are unable to raise sufficient capital to fund our planned operations, we may be forced to curtail operations and/or explore strategic alternatives, including a sale of the company or a merger.

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

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings and debt financings. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of common stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of common stockholders. Debt financing and preferred equity 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.

We cannot be certain that additional funding will be available on acceptable terms, or at all. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts.

Future sales of shares by existing stockholders could cause the Company's stock price to decline.

If existing stockholders of the Company sell, or indicate an intention to sell, substantial amounts of the Company's common stock in the public market the trading price of the common stock of the combined company could decline. At December 31, 2019, the Company had approximately 13.0 million shares outstanding.

Risks Related to Regulatory Approval of Our Product Candidates and Other Legal Compliance Matters

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, or the approvals may be for a narrow indication, we may not be able to commercialize our product candidates, and our ability to generate revenue may be materially impaired.

Our product candidates must be approved by the FDA pursuant to a new drug application in the United States and by other regulatory authorities outside the United States prior to commercialization in the respective regions. The process of obtaining marketing approvals, both in the United States and outside the United States, is expensive and takes several years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not received approval to market any of our product candidates from regulatory authorities in any country. We have no experience in filing and supporting the applications necessary to gain marketing approvals for ENT products and may engage third-party consultants to assist in this process. Securing marketing approval requires the submission of extensive nonclinical and clinical data, and other supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product formulation and manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional nonclinical, clinical or other data. In addition, varying interpretations of the data obtained from nonclinical and clinical trials could delay, limit or prevent marketing approval of a product candidate. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may also cause delays in or prevent the approval of an application.

Any marketing approval we ultimately obtain may be for fewer or more limited indications than requested or subject to restrictions or post-approval commitments that render the approved product not commercially viable or its market potential significantly impaired. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

Failure to obtain marketing approval in international jurisdictions would prevent our product candidates from being marketed outside the United States

In order to market and sell our products in the EU and other international jurisdictions outside of the United States, we or our third-party collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and may require additional nonclinical, clinical or health outcome data. In addition, the time required to obtain approval may differ substantially amongst international jurisdictions. The regulatory approval process outside the United States generally includes all the risks associated with obtaining FDA approval. In addition to regulatory approval, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or these third parties may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the EMA, MHRA, or FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

Any product candidate for which we obtain marketing approval will be subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Our product candidates and the activities associated with their development and commercialization, including their testing, manufacture, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation that are specific to those defined by regulatory authorities in the countries where the product is approved. In the United States and other countries that follow the International Conference on Harmonization, these requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, including periodic inspections by the FDA and other regulatory authorities, requirements regarding the distribution of samples to physicians and recordkeeping.

The FDA, or other regulatory authorities, may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding use of their products and if we promote our products beyond their approved indications, we may be subject to enforcement action for off-label promotion. Violations of the Federal Food, Drug, and Cosmetic Act relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Non-compliance with EU requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the EU's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Legislation regulating the pharmaceutical and healthcare industries may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes intended to contain healthcare costs and modify the regulation of drug and biologic products. These and other regulatory changes could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

For example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act (collectively, the "PPACA") substantially changed the way healthcare is financed by both governmental and private insurers, significantly impacting the U.S. pharmaceutical industry. The PPACA, among other things, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for certain drugs, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, and establishes annual fees and taxes on manufacturers of certain branded prescription drugs. Implementation of the PPACA remains ongoing, but there is uncertainty as to how the law's various provisions will ultimately affect the industry and whether all aspects of the law will remain in place.

In addition to the PPACA, other legislative changes have been proposed and adopted since the PPACA was enacted. In the United States, the Budget Control Act of 2011 included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013. This policy was initially set to expire in fiscal year 2021 but has been extended to 2025. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Further, under the Trump administration there may be additional regulatory changes, as well as the potential repeal (in whole or in part) of the PPACA, that could negatively affect insurance coverage and/or drug prices. Any such new laws may result in additional reductions in Medicare and other healthcare funding.

We expect that the PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government 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.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

We expect that additional state and federal healthcare reform measures and regulations will be adopted in the future. Any of these measures and regulations could limit the amounts that federal and state governments will pay for healthcare products and services, result in reduced demand for our product candidates or additional pricing pressures and affect our product development, testing, marketing approvals and post-market activities.

Laws, restrictions, and other regulatory measures are also imposed by healthcare laws and regulations in international jurisdictions and in those jurisdictions we face the same issues as in the United States regarding difficulty and cost for us to obtain marketing approval and commercialization of our product candidates and which may affect the prices we may obtain.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, particularly the countries of the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

Our business operations and relationships with healthcare providers, physicians, third-party payers, and customers will be subject to applicable anti-kickback, fraud and abuse and other broadly applicable healthcare laws, which could expose us to criminal sanctions, civil penalties, program exclusion, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payers will play a primary role in the recommendation and prescription of any product candidates for which we receive marketing approval. Our current and future arrangements may expose us to broadly applicable fraud and abuse and other healthcare laws that may constrain the business or financial arrangements and relationships through which we would market, sell and distribute the products for which we receive marketing approval. Even though we will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payers, federal and state healthcare laws are and will be applicable to our business. Such laws include, but are not limited to, the following:

- federal false claims, false statements and civil monetary penalties laws, including the federal civil False Claims Act ("FCA"), which can be enforced through civil whistleblower or qui tam actions, prohibit, among others, any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, or causing to be made, a false statement to get a false claim paid.
- the federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers, on the one hand, and prescribers, purchasers and formulary managers, on the other. Although there are several statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution, the exceptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. In addition, the intent standard under the federal Anti-Kickback Statute was amended by the Affordable Care Act to a stricter standard 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. Moreover, 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;
- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") which prohibits, among other things, knowingly and willfully executing, or attempting to execute, a scheme or artifice to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private), willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false, fictitious or fraudulent statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- patient data privacy and security regulation, including, in the United States, HIPAA, as amended by the Health Information Technology for Clinical Health Act of 2009 ("HITECH"), and their respective implementing regulations, which impose specified requirements on "covered entities," including healthcare providers, health plans, and healthcare clearinghouses, as well as their respective "business associates" that perform services for them that involve the use, or disclosure of, individually identifiable health information relating to the privacy, security and transmission of individually identifiable health information.
- the federal transparency requirements under the Physician Payments Sunshine Act, enacted as part of the Affordable Care Act, that require applicable manufacturers of covered drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to track and annually report to the Centers for Medicare & Medicaid Services ("CMS"), an agency within the U.S. Department of Health and Human Services, payments and other transfers of value provided to physicians and teaching hospitals and certain ownership and investment interests held by physicians or their immediate family members in the applicable manufacturer, and disclosure of such information will be made by CMS on a publicly available website.

- analogous state, local or foreign laws, such as state anti-kickback and false claims laws, which may apply to items or services reimbursed by any third-party payor, including commercial insurers; state and local marketing and/or transparency laws applicable to manufacturers that may be broader in scope than the federal requirements; state laws that require biopharmaceutical companies to comply with the biopharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state and local laws that require licensure or registration by sales and marketing agents of a pharmaceutical company; state laws that require disclosure of information related to drug pricing; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect as HIPAA.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures.

State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. The global data protection landscape is rapidly evolving, and we may be affected by or subject to new, amended or existing laws and regulations in the future, including as our operations continue to expand or if we operate in foreign jurisdictions. For example, in June 2018, California enacted the California Consumer Privacy Act of 2018 (the "CCPA"), which took effect on January 1, 2020. The CCPA gives California residents the right to access and require deletion of their personal information, the right to opt out of certain personal information sharing, and the right to detailed information about how their personal information is collected, used and shared. The CCPA provides civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Although the CCPA includes exemptions for certain clinical trials data, the law may increase our compliance costs and potential liability with respect to other personal information we collect about California residents. The CCPA has prompted a wave of proposals for new federal and state privacy legislation that, if passed, could increase our potential liability, increase our compliance costs and adversely affect our business. Several foreign jurisdictions, including the EU, its member states, the United Kingdom, Japan and Australia, among others, have adopted legislation and regulations that increase or change the requirements governing the collection, use, disclosure and transfer of the personal information of individuals in these jurisdictions. Additionally, certain countries have passed or are considering passing laws that require local data residency and/or restrict the international transfer of data. These laws have the potential to increase costs of compliance, risks of noncompliance and penalties for noncompliance.

Pharmaceutical and other healthcare companies have been prosecuted under these laws for a variety of promotional and marketing activities, such as: providing free trips, free goods, sham consulting fees and grants and other monetary benefits to prescribers; reporting to pricing services inflated average wholesale prices that were then used by federal programs to set reimbursement rates; engaging in off-label promotion; and submitting inflated best price information to the Medicaid Rebate Program to reduce liability for Medicaid rebates. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations.

If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, disgorgement, fines, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, additional oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, that person or entity may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Laws, restrictions, and other regulatory measures are also imposed by anti-kickback, fraud and abuse, and other healthcare laws and regulations in international jurisdictions, and in those jurisdictions we face the same issues as in the United State regarding exposure to criminal sanctions, civil penalties, program exclusion, contractual damages, reputational harm, and diminished profits and future earnings.

We depend on our information technology systems and those of our third-party collaborators, service providers, contractors or consultants. Our internal computer systems, or those of our third-party collaborators, service providers, contractors or consultants, may fail or suffer security breaches, disruptions, or incidents, which could result in a material disruption of our development programs or loss of data or compromise the privacy, security, integrity or confidentiality of sensitive information related to our business and have a material adverse effect on our reputation, business, financial condition or results of operations.

In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. Our internal technology systems and infrastructure, and those of our current or future third-party collaborators, service providers, contractors and consultants are vulnerable to damage from computer viruses, unauthorized access or use resulting from malware, natural disasters, terrorism, war and telecommunication and electrical failures, denial-of-service attacks, cyber-attacks or cyber-intrusions over the Internet, hacking, phishing and other social engineering attacks, persons inside our organizations (including employees or contractors), loss or theft, or persons with access to systems inside our organization. Attacks on information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and they are being conducted by increasingly sophisticated and organized foreign governments, groups and individuals with a wide range of motives and expertise. In addition to extracting or accessing sensitive information, such attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the security, confidentiality, integrity and availability of information. The prevalent use of mobile devices that access sensitive information also increases the risk of data security incidents which could lead to the loss of confidential information or other intellectual property. While to our knowledge we have not experienced any material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations or the operations of third-party collaborators, service providers, contractors and consultants, it could result in a material disruption of our development programs and significant reputational, financial, legal, regulatory, business or operational harm. The costs to us to mitigate, investigate and respond to potential security incidents, breaches, disruptions, network security problems, bugs, viruses, worms, malicious software programs and security vulnerabilities could be significant, and while we have implemented security measures to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service and other harm to our business and our competitive position.

For example, the loss of clinical trial data from completed, ongoing or planned clinical trials for our product candidates 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 real or perceived security breach affects our systems (or those of our third-party collaborators, service providers, contractors or consultants), or results in the loss of or accidental, unlawful or unauthorized access to, use of, release of, or other processing of personally identifiable information or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed. Such a breach may require notification to governmental agencies, the media or individuals pursuant to various foreign, domestic (federal and state) privacy and security laws, if applicable, including HIPAA, as amended by HITECH, and its implementing rules and regulations, as well as regulations promulgated by the Federal Trade Commission and state breach notification laws. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyberattacks and other related incidents.

Any failure or perceived failure by us or any third-party collaborators, service providers, contractors or consultants to comply with our privacy, confidentiality, data security or similar obligations, or any data security incidents or other security breaches that result in the accidental, unlawful or unauthorized access to, use of, release of, processing of, or transfer of sensitive information, including personally identifiable information, may result in negative publicity, harm to our reputation, governmental investigations, enforcement actions, regulatory fines, litigation or public statements against us, could cause third parties to lose trust in us or could result in claims by third parties, including those that assert that we have breached our privacy, confidentiality, data security or similar obligations, any of which could have a material adverse effect on our reputation, business, financial condition or results of operations. To the extent we maintain individually identifiable health information, we could be subject to fines and penalties (including civil and criminal) under HIPAA for any failure by us or our business associates to comply with HIPAA's requirements. Moreover, data security incidents and other security breaches can be difficult to detect, and any delay in identifying them may lead to increased harm. While we have implemented data security measures intended to protect our information, data, information technology systems, applications and infrastructure, there can be no assurance that such measures will successfully prevent service interruptions or data security incidents.

European data collection is governed by restrictive regulations governing the collection, use, processing and cross-border transfer of personal information.

We may collect, process, use or transfer personal information from individuals located in the European Economic Area in connection with our business, including in connection with conducting clinical trials in the EEA. Additionally, if any of our product candidates are approved, we may seek to commercialize those products in the European Economic Area. The collection and use of personal health data in the European Economic Area is governed by the provisions of the General Data Protection Regulation ((EU) 2016/679) (the "GDPR"), along with other European Union and country-specific laws and regulations. The United Kingdom and Switzerland have also adopted data protection laws and regulations. These legislative acts (together with regulations and guidelines) impose requirements relating to having legal bases for processing personal data relating to identifiable individuals and transferring such data outside of the European Economic Area, including to the United States, providing details to those individuals regarding the processing of their personal data, keeping personal data secure, having data processing agreements with third parties who process personal data, responding to individuals' requests to exercise their rights in respect of their personal data, reporting security breaches involving personal data to the competent national data protection authority and affected individuals, appointing data protection officers or corporate representatives, conducting data protection impact assessments and record-keeping. The GDPR imposes additional responsibilities and liabilities in relation to personal data that we process and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. Failure to comply with the requirements of the GDPR and related national data protection laws of the member states of the European Economic Area and other states in the European Economic Area may result in substantial fines, other administrative penalties and civil claims being brought against us, which could have a material adverse effect on our business, financial condition and results of operations. European data protection authorities may interpret the GDPR and national laws differently and may impose additional requirements, which adds to the complexity of processing personal data in or from the EEA or United Kingdom. Guidance on implementation and compliance practices are often updated or otherwise revised.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our nonclinical or clinical development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to the Commercialization of Our Product Candidates

Even if any of our product candidates receives marketing approval, we may fail to achieve the degree of market acceptance by physicians, patients, third-party payers and others in the medical community necessary for commercial success.

If any of our product candidates receives marketing approval, we may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payers and others in the medical community. In addition, physicians, patients and third-party payers may prefer other novel products to ours. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety and potential advantages and disadvantages compared to alternative treatments;
- the ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of our marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement, including patient cost-sharing programs such as copays and deductibles;
- the ability to develop or partner with third-party collaborators to develop companion diagnostics;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our products together with other medications.

If our current product candidates, or a future product candidate receives marketing approval and we, or others, later discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, the ability to market the product could be compromised.

Clinical trials are conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials may indicate an apparent beneficial effect of a product candidate that is greater than the actual positive effect in a broader patient population or alternatively fail to identify undesirable side effects. If, following approval of a product candidate, we, or others, discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following events could occur:

- regulatory authorities may withdraw their approval of the product or seize the product;
- the product may be required to be recalled or changes may be required to the way the product is administered;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the product;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- the creation of a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- additional restrictions may be imposed on the distribution or use of the product via a Risk Evaluation and Mitigation Strategy;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Any of these events could have a material and adverse effect on our operations and business. The commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

We currently have no marketing and sales force. If we are unable to establish effective marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, we may not be able to effectively market and sell our product candidates, if approved, or generate product revenues.

We currently do not have a marketing or sales team for the marketing, sales and distribution of any of our product candidates that are able to obtain regulatory approval. In order to commercialize any product candidates, we must build on a territory-by-territory basis marketing, sales, distribution, 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 product candidates receive regulatory approval, we intend to establish an internal sales and marketing team with technical expertise and supporting distribution capabilities to commercialize our product candidates, which will be expensive and time-consuming, will require significant attention of our executive officers to manage and may nonetheless fail to effectively market and sell our product candidates. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of any of our products that we obtain approval to market. With respect to the commercialization of all or certain of our product candidates, we may choose to collaborate, either globally or on a territory-by-territory basis, with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. If we are unable to enter into such arrangements when needed on acceptable terms or at all, we may not be able to successfully commercialize any of our product candidates that receive regulatory approval, or any such commercialization may experience delays or limitations. If we are not successful in commercializing our product candidates, either on our own or through collaborations with one or more third parties, our future product revenue will suffer, and we may incur significant additional losses.

We face substantial competition, which may result in others discovering, developing or commercializing competing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are several large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we are developing our product candidates. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

Specifically, there are a number of companies developing or marketing treatments for AOE, including many major pharmaceutical and biotechnology companies. We expect that OP0102 will face competition from numerous FDA-approved therapeutics, including CIPRODEX® and numerous other branded and generic ear anti-infectives.

In OM, there are currently no drug therapies approved for the treatment or prevention of OM. We expect that OP0201 will compete primarily with a surgery where the tympanic membrane is perforated to improve drainage and ventilation of the middle ear (myringotomy or tympanostomy tube insertions) as a means of preventing recurrent or chronic OM. We may also compete with a medical device that uses a small intranasal balloon inserted into the ET to ventilate the ET in patients with ETD of a particular type. Surgery may continue to be the preferred treatment for OM in children whereas the intranasal balloon may be the preferred treatment for ET dysfunction in adults. Patients may be prescribed concurrent antibiotic therapy for AOM, but these products will not be competitive with, but likely used in conjunction with OP0201.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. In addition, our ability to compete may be affected in many cases by insurers or other third-party payers seeking to encourage the use of generic products.

Generic products are currently available, with additional products expected to become available over the coming years, potentially creating pricing pressure. If our product candidates achieve marketing approval, we expect that they will be priced at a significant premium over competitive generic products.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, conducting nonclinical studies, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

The insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for new or current products could limit our ability to market those products and decrease our ability to generate revenue.

The availability and extent of reimbursement by governmental and private payers is essential for most patients to be able to afford expensive treatments. Sales of our product candidates will depend substantially, both domestically and internationally, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payers. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about reimbursement for new medicines are typically made by CMS, as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private payers tend to follow CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for fundamentally novel products such as ours, as there is no body of established practices and precedents for these new products. Reimbursement agencies in Europe may be more conservative than CMS. Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, and other countries has and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medicines but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenues and profits.

Moreover, increasing efforts by governmental and third-party payers, in the United States and internationally, to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. Increased expense is incurred to cover costs of health outcome focused research used to generate data necessary to justify the value of our products in order to secure reimbursement. We expect to experience pricing pressures in connection with the sale of any of our product candidates, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products into the healthcare market.

In addition, many private payers contract with commercial vendors who sell software that provide guidelines that attempt to limit utilization of, and therefore reimbursement for, certain products deemed to provide limited benefit to existing alternatives. Such organizations may set guidelines that limit reimbursement or utilization of our products.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. If we cannot successfully defend against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

We currently hold $5.0 million in product liability insurance coverage in the aggregate, with a per incident limit of $5.0 million, which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Our business could be adversely affected by natural disasters, public health epidemics, and other events beyond our control.

Our business could be adversely affected by the recent coronavirus outbreak (COVID-19) which has affected more than 100 countries and has significantly disrupted the day-to-day activities of both individuals and businesses. We rely on consultants and third party organizations around the world to supply goods, develop and manufacture drug product, and execute clinical trials. We may experience time delays and incur unplanned expenses as a result of the impact of the ongoing COVID-19 pandemic.

Risks Related to Our Dependence on Third Parties

Future development collaborations may be important to us. If we are unable to enter into or maintain these collaborations, or if these collaborations are not successful, our business could be adversely affected.

For some of our product candidates, we may in the future determine to seek to collaborate with pharmaceutical and biotechnology companies for development or commercialization of our product candidates. We face significant competition in seeking appropriate collaborators. Our ability to reach a definitive agreement for any collaboration will depend, among other things, upon our assessment of the collaborator’s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator’s evaluation of several factors. If we are unable to reach agreements with suitable

collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential development schedule or reduce the scope of research activities, or increase our expenditures and undertake discovery or nonclinical development activities at our own expense. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development activities, we may not be able to further develop our product candidates or continue to develop our product candidates, and our business may be materially and adversely affected.

Future collaborations that we may enter could involve the following risks:

- collaborators may have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, may divert resources or create competing priorities;
- collaborators may delay discovery, nonclinical or clinical development, provide insufficient funding for product development of targets selected by us, stop or abandon discovery, nonclinical or clinical development for a product candidate, or repeat or conduct new discovery, and nonclinical and clinical development for a product candidate;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed than our products;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the development of our product candidates;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the discovery, nonclinical or clinical development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or intellectual property rights licensed to us or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Additionally, subject to its contractual obligations to us, if a collaborator is involved in a business combination, the collaborator might deemphasize or terminate the development of any of our product candidates. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected.

If our collaborations do not result in the successful development of products or product candidates, product candidates could be delayed, and we may need additional resources to develop product candidates. All of the risks relating to product development, regulatory approval and commercialization described in this periodic report also apply to the activities of our collaborators.

We contract with third parties for the manufacture of our product candidates for nonclinical and clinical trials and expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products at an acceptable cost and quality, which could delay, prevent or impair our development or commercialization efforts.

We have utilized, and intend to continue utilizing, third parties to formulate, manufacture, package, and distribute clinical supplies of our drug candidates. We have no experience in manufacturing and do not have any manufacturing facilities. Currently, we have sole suppliers for one or more of our active pharmaceutical ingredients ("API"), and a different sole manufacturer for each of our product candidates. In addition, these materials are custom-made and available from only a limited number of sources. In particular, there may be a limited supply source for APIs for OP0201 or other potential product candidates. Although we

believe that our third-party suppliers maintain a significant supply of APIs on hand, any sustained disruption in this supply could adversely affect our operations. We do not have any long-term agreements in place with our current API suppliers. If we are required to change manufacturers, we may experience delays associated with finding an alternate manufacturer that is properly qualified to produce supplies of our products and product candidates in accordance with regulatory requirements and our specifications. Any delays or difficulties in obtaining APIs or in manufacturing, packaging or distributing approved product candidates could negatively affect our sales revenues, as well as delay our clinical trials.

We expect to rely on third-party manufacturers or third-party collaborators for the manufacture of commercial supply of any other product candidates for which our collaborators or we obtain marketing approval. Despite drug substance and product risk management, this reliance on third parties presents a risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts. Any performance failure on the part of our existing or future manufacturers of drug substance or drug products could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply. If suppliers cannot supply us with our requirements, we may be required to identify alternative manufacturers, which would lead us to incur added costs and delays in identifying and qualifying any such replacement.

Formulations and devices used in early studies are not final formulations and devices for commercialization. Additional changes may be required by the FDA or other regulatory authorities on specifications and storage conditions. These may require additional studies and may result in a delay in our clinical trials and commercialization activities.

We also expect to rely on other third parties to label, store, and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

We may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

The third parties we rely on for manufacturing and packaging are also subject to regulatory review, and any regulatory compliance problems with these third parties could significantly delay or disrupt our clinical or commercialization activities. Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. Additionally, macro-economic conditions may adversely affect these third parties, causing them to suffer liquidity or operational problems. If a key third-party vendor becomes insolvent or is forced to lay off workers assisting with our projects, our results and development timing could suffer.

Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

We depend on CROs and other contracted third parties to perform nonclinical and clinical testing and certain other research and development activities. As a result, the outcomes of the activities performed by these organizations will be, to a certain extent, beyond our control.

The nature of outsourcing a substantial portion of our business will require that we rely on CROs and other contractors to assist us with research and development, clinical testing activities, patient enrollment, data collection, and regulatory submissions to the FDA or other regulatory bodies. As a result, our success will depend partially on the success of these third

parties in performing their responsibilities. Although we intend to pre-qualify our CROs and other contractors and we believe that the contractors selected will be fully capable of performing their contractual obligations, we cannot directly control the adequacy and timeliness of the resources and expertise that they apply to these activities. Additionally, macro-economic conditions may affect our development partners and vendors, which could adversely affect their ability to timely perform their tasks. If our contractors do not perform their obligations in an adequate and timely manner, the pace of clinical development, regulatory approval and commercialization of our drug candidates could be significantly delayed, and our prospects could be adversely affected.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain intellectual property protection for our technology and products or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be impaired.

Our success depends in large part on our ability to obtain and maintain patent protection in the EU, the United States and other countries with respect to our proprietary technology and products. We seek to protect our proprietary position by filing patent applications in the United States and internationally that are related to our novel technologies and product candidates. This patent portfolio includes issued patents and pending patent applications covering pharmaceutical compositions and methods of use.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. We may choose not to seek patent protection for certain innovations and may choose not to pursue patent protection in certain jurisdictions, and under the laws of certain jurisdictions, patents or other intellectual property rights may be unavailable or limited in scope. It is also possible that we will fail to identify patentable aspects of our discovery and nonclinical development output before it is too late to obtain patent protection. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, India and China do not allow patents for methods of treating the human body. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the EU, the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. On September 16, 2011, the Leahy-Smith America Invents Act (the “Leahy-Smith Act”), was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The U.S. Patent and Trademark Office (“USPTO”) recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

Moreover, we may be subject to a third-party pre-issuance submission of prior art to the USPTO, or become involved in opposition, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without

infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner.

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 the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product 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 products similar or identical to our own.

The risks described elsewhere pertaining to our patents and other intellectual property rights also apply to the intellectual property rights that we license, and any failure to obtain, maintain and enforce these rights could have a material adverse effect on our business. In some cases, we may not have control over the prosecution, maintenance or enforcement of the patents that we license, and our licensors may fail to take the steps that we believe are necessary or desirable in order to obtain, maintain and enforce the licensed patents. Any inability on our part to protect adequately our intellectual property may have a material adverse effect on our business, operating results and financial position.

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

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. The USPTO and various non-U.S. governmental patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. In certain situations, non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

If we fail to comply with our obligations in the agreements under which we license intellectual property and other rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We have acquired rights to our surfactant platform through a license agreement with Otodyne, Inc. and may in the future enter into other license agreements with third parties for other intellectual property rights or assets. These license agreements may impose various diligence, milestone payment, royalty, and other obligations on us. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, we may be required to make certain payments to the licensor, we may lose the exclusivity of our license, or the licensor may have the right to terminate the license, in which event we would not be able to develop or market products covered by the license. Additionally, the milestone and other payments associated with these licenses will make it less profitable for us to develop our drug candidates than if we had developed the licensed technology internally.

In some cases, patent prosecution of our licensed technology may be controlled solely by the licensor. If our licensors fail to obtain and maintain patent or other protection for the proprietary intellectual property we license from them, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, and our competitors could market competing products using the intellectual property. In certain cases, we may control the prosecution of patents resulting from licensed technology. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners. If disputes over intellectual property and other rights that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time-consuming and unsuccessful.

Because competition in our industry is intense, competitors may infringe or otherwise violate our issued patents, patents of our licensors or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly, or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. We may also elect to enter into license agreements in order to settle patent infringement claims or to resolve disputes prior to litigation, and any such license agreements may require us to pay royalties and other fees that could be significant. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure.

We may need to license certain intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property, including patent rights, that are important or necessary to the development of our products. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties on commercially reasonable terms, or our business could be harmed, possibly materially. If we were not able to obtain a license, or are not able to obtain a license on commercially reasonable terms, our business could be harmed, possibly materially.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference or derivation proceedings before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. Any NDAs or similar agreements entered into by the Company may not be with all relevant parties, or adequately protect the confidentiality of our trade secrets. Moreover, to the extent we enter into such agreements, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate them, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

Risks Related to Our Employee Matters, Managing Growth and Macroeconomic Conditions

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

We are highly dependent on the product development, clinical and business development expertise of the principal members of our management, scientific and clinical team. Although we have entered into employment agreements with our executives and key employees, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees.

Recruiting and retaining qualified scientific, clinical, manufacturing, sales and marketing personnel is critical to our success. Due to the small size of the Company and the limited number of employees, each of our executives and key employees serves in a critical role. The loss of the services of our executive officers or other key employees could impede the achievement of our development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of, and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating drug product, nonclinical development, clinical development, regulatory strategy, and commercial strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to provide services to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We expect to expand our research and development function, as well as our corporate operations, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

To successfully develop and commercialize any of our product candidates, we will need to increase the number of our employees and the scope of our operations, in areas such as research and development, medical and regulatory affairs, manufacturing, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

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

Many of our employees and certain of our directors were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees and directors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees or directors have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's or director's former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

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

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. A severe or prolonged economic downturn, such as the recent global financial crisis, could result in a variety of risks to our business, including our ability to raise additional capital when needed on acceptable terms, if at all. This is particularly true in Europe, where the United Kingdom's vote to leave the EU has created additional economic uncertainty. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

Risks Related to Our Common Stock

We expect our stock price to be volatile, and the market price of our common stock may drop unexpectedly.

The market price of our common stock could be subject to significant fluctuations. Market prices for securities of early-stage pharmaceutical, biopharmaceutical, 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 or other product candidates, and delays or failures to obtain such approvals;
- failure of any of our product candidates, if approved, to achieve commercial success;
- issues in manufacturing our approved products, if any, or product candidates;
- the results of our current and any future clinical trials of our product candidates;
- the entry into, or termination of, key agreements, including key commercial partner agreements;
- the initiation of, material developments in, or conclusion of litigation to enforce or defend any of our intellectual property rights or defend against the intellectual property rights of others;
- announcements by commercial partners or competitors of new commercial products, clinical progress or the lack thereof, significant contracts, commercial relationships or capital commitments;
- the introduction of technological innovations or new therapies that compete with our potential products;
- the loss of key employees;
- changes in estimates or recommendations by securities analysts, if any, who cover our common stock;
- general and industry-specific economic conditions that may affect our research and development expenditures;
- changes in the structure of healthcare 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 are not currently in compliance with the continued listing requirements for Nasdaq. If the price of our common stock continues to trade below $1.00 per share for a sustained period or we do not meet other continued listing requirements, our common stock may be delisted from the Nasdaq Capital Market, which could affect the market price and liquidity for our common stock and reduce our ability to raise additional capital.

On August 8, 2019, we received written notice (the "Notification Letter") from The Nasdaq Stock Market LLC ("Nasdaq") notifying us that the Company was not in compliance with the minimum bid price requirements set forth in Nasdaq Listing Rule 5550(a)(2) for continued listing on the Nasdaq Capital Market. Nasdaq Listing Rule 5550(a)(2) requires listed securities maintain a minimum closing bid price of $1.00 per share, and Nasdaq Listing Rule 5810(c)(3)(A) provides that a failure to meet the minimum closing bid price requirement exists if the deficiency continues for a period of 30 consecutive business days. Based on the closing bid price of the Company's common stock for the 30 consecutive business days prior to the date of the Notification Letter, the we did not meet the minimum closing bid price requirement.

On February 6, 2020, we received written notice that Nasdaq determined that we are eligible for an additional 180-day extension (the "Extension Letter"), or until August 3, 2020, to regain compliance with the minimum bid price requirement. The Extension Letter does not impact the Company's listing on the Nasdaq Capital Market at this time. To regain compliance, the closing bid price of the Company's common stock must be at least $1.00 per share for a minimum of 10 consecutive business days at any time prior to August 3, 2020.

We intend to monitor the closing bid price of our common stock and consider our available options to resolve our noncompliance with the minimum bid price requirement. There can be no assurance that we will be able to regain compliance with the minimum bid price requirement or we will otherwise be in compliance with other Nasdaq listing criteria. If we fail to regain compliance with the minimum bid requirement or to meet the other applicable continued listing requirements for the Nasdaq Capital Market in the future and Nasdaq determines to delist our common stock, the delisting could adversely affect the market price and liquidity of our common stock and reduce our ability to raise additional capital.

If our common stock is delisted by Nasdaq, our common stock may be eligible to trade on the OTC Bulletin Board or another over-the-counter market. Any such alternative would likely result in it being more difficult for us to raise additional capital through the public or private sale of equity securities and for investors to dispose of, or obtain accurate quotations as to the market value of, the common stock and could result in a decrease in the trading price of our common stock. In addition, there can be no assurance that the common stock would be eligible for trading on any such alternative exchange or markets.

If securities analysts do not publish research or reports about our business, or if they publish negative evaluations, the price of our common stock could decline.

The trading market for our common stock may be impacted by the availability or lack of research and reports that third-party industry or financial analysts publish about the Company. There are many large, publicly traded companies active in the biopharmaceutical industry, which may mean it will be less likely that we receive widespread analyst coverage. Furthermore, if one or more of the analysts who do cover the Company downgrade our stock, our stock price would likely decline. If we do not receive adequate coverage by reputable analysts that have an understanding of our business and industry, we could fail to achieve visibility in the market, which in turn could cause our stock price to decline.

Our executive officers, directors and principal stockholders, if they choose to act together, will have the ability to control all matters submitted to stockholders for approval.

Our executive officers and directors, combined with our principal stockholders, beneficially own shares representing approximately 70.7% of our capital stock as of December 31, 2019. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of ownership control may:

- delay, defer or prevent a change in control;
- entrench our management and the board of directors; or
- impede a merger, consolidation, takeover or other business combination involving the Company that other stockholders may desire.

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

As a public company, we incur significant legal, accounting and other expenses that we did not previously incur as a private company, including costs associated with public company reporting requirements. We will also incur costs associated with corporate governance requirements, including requirements under the Sarbanes-Oxley Act and rules and regulations promulgated by the SEC and Nasdaq. These rules and regulations are expected to increase our legal and financial compliance costs and to make some activities more time-consuming and costly. These rules and regulations may also make it difficult and expensive for the Company to obtain directors' and officers' liability insurance. As a result, it may be more difficult for the Company to attract and retain qualified individuals to serve on our board of directors or as executive officers of the Company, which may adversely affect investor confidence in the Company and could cause our business or stock price to suffer.

If we fail to establish and maintain proper and effective internal control over financial reporting, our operating results and our ability to operate our business could be harmed.

Ensuring that we will have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. 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 in accordance with accounting principles generally accepted in the United States ("GAAP").

Our financial statements have only been prepared in accordance with GAAP since May 2017. Since that time, we have implemented measures designed to improve our internal controls over financial reporting, including by bringing in additional accounting resources and establishing new accounting and financial reporting procedures to establish an appropriate level of internal controls over financial reporting. If we are unable to successfully maintain internal controls over financial reporting, the accuracy and timing of our financial reporting, and our stock price, may be adversely affected and we may be unable to maintain compliance with the applicable stock exchange listing requirements.

Implementing any appropriate changes to our internal controls may distract the officers and employees of the Company, entail substantial costs to modify its existing processes and take significant time to complete. These changes may not, however, be effective in maintaining the adequacy of the internal controls of the Company, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase operating costs and harm the business. In addition, investors' perceptions that the internal controls of the Company are inadequate or that we are unable to produce accurate financial statements on a timely basis may harm the stock price of the Company.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of the Company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our corporate charter and bylaws may discourage, delay or prevent a merger, acquisition or other change in control of the Company that stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because the board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by stockholders to replace or remove the current management by making it more difficult for stockholders to replace members of the board of directors. Among other things, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize the board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of the Company's charter or bylaws.

Moreover, because the Company is incorporated in Delaware, it is governed by the provisions of Section 203 of the DGCL, which prohibits a person who owns in excess of 15% of its outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

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

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

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 2. Properties.

Our executive offices are located in Irvine, California. We lease approximately 5,197 square feet of office space under an operating lease that expires in September 2021.

Item 3. Legal Proceedings.

Information pertaining to legal proceedings is provided under the heading “Legal Proceedings” in Note 5, Commitments and Contingencies, to the consolidated financial statements and is incorporated by reference herein.

Item 4. Mine Safety Disclosures.

None.

PART II

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

Market Information

Our common stock is traded on the Nasdaq Capital Market under the symbol "NVUS".

As of March 9, 2020, there were approximately 11 stockholders of record of our common stock.

Dividends

We have never declared or paid, and do not anticipate declaring or paying in the foreseeable future, any cash dividends on our common stock. Future determination as to the declaration and payment of dividends, if any, will be at the discretion of our board of directors and will depend on then existing conditions, including our operating results, financial condition, contractual restrictions, capital requirements, business prospects and other factors that our board of directors may deem relevant.

Item 6. Selected Financial Data.

Per §229.301 of Regulation S-K, the Company, designated a Smaller Reporting Company as defined in §229.10(f)(1) of Regulation S-K, is not required to provide the disclosure required by this Item.

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

Management's Discussion and Analysis of Financial Condition and Results of Operations is intended to help the reader understand the results of operations and financial condition of the Company. The Management's Discussion and Analysis of Financial Condition and Results of Operations should be read in conjunction with our audited consolidated financial statements and notes thereto for the year ended December 31, 2019. In addition to historical information, this Annual Report on Form 10-K contains 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, which are intended to be covered by the safe harbors created thereby. See "Cautionary Note Regarding Forward-Looking Statements" in this report. Our actual results and the timing of events could differ materially from those discussed in our forward-looking statements as a result of many factors, including those set forth under the Part I, Item 1A. Risk Factors section and elsewhere in this report, as well as, in other reports and documents we file with the Securities and Exchange Commission from time to time. Except as required by law, we undertake no obligation to update any forward-looking statements to reflect events or circumstances occurring after the date of this Annual Report on Form 10-K.

ABOUT NOVUS THERAPEUTICS

Overview

Novus Therapeutics, Inc. is a specialty pharmaceutical company focused on developing products for patients with disorders of the ear, nose, and throat. The Company has two platform technologies, a surfactant and a foam, each with the potential to be developed for multiple indications. Novus' lead program, OP0201, is a surfactant-based nasal aerosol drug-device combination product candidate being developed as a potential first-in-class treatment option for patients at risk for, or with, otitis media ("OM"). OM is defined as middle ear inflammation and effusion with or without infection. Globally, OM affects more than 700 million adults and children every year, with over half of the cases occurring in children under five years of age. OM is one of the most common disorders seen in pediatric practice, and is a leading cause of health care visits and the most frequent reason children are prescribed antibiotics or undergo surgery in the United States. Novus also has a foam-based drug delivery technology platform, which may be developed in the future to deliver drugs into the ear, nasal, and sinus cavities.

Surfactant Platform

The first product in the surfactant platform program, OP0201, is being developed as a potential first-in-class treatment option for OM. OM is often caused by Eustachian tube dysfunction ("ETD"). OP0201 is a nasal aerosol, drug-device combination product comprised of a novel formulation of a surfactant (dipalmitoylphosphatidylcholine ("DPPC")) and a spreading agent (cholesteryl palmitate ("CP")) suspended in propellant. The product is administered intranasally via a pressurized metered-dose inhaler ("pMDI"). OP0201is intended to be used to restore the normal physiologic activity of the Eustachian tube ("ET"), which is a small tube that connects from the chamber of the middle ear to the back of the nasopharynx. Together, the active ingredients in OP0201 effectively absorb to the air-liquid interface of the mucosa and reduce the interfacial surface tension of the ET, which reduces passive pressure required for the ET to open. In other words, OP0201 promotes 'de-sticking' of the ET so that ventilation of the middle ear is restored. Novus is also exploring the use of a dry-powder unit dose device as an alternative option for intranasal administration of DPPC and CP

Novus has completed three phase 1 placebo-controlled clinical trials in adults that were designed to evaluate safety and tolerability of single and repeated intranasal doses of OP0201. Results of a single-dose phase 1 trial in healthy adults (study C-001), a single-dose phase 1 trial in adults with acute otitis media (study C-004), and a 14-day phase 1 trial in healthy adults (study C-002) demonstrated the safety and tolerability of OP0201 nasal aerosol. Novus is currently conducting an exploratory phase 2a clinical trial of OP0201 nasal aerosol in infants and children with acute otitis media (study C-006).

Novus' surfactant development program, if successful, will lead to registration of a surfactant-based product in North America and key European markets to treat and/or prevent OM in infants and children. Additional development activities to support registration in other countries, or for other indications, or other patient populations, may occur in the future.

Foam Platform

Novus has two product candidates developed, OP0101 and OP0102, which are foam-based product candidates intended to be used as a delivery vehicle for drugs to be administered into the ear canals, as well as the nasal and sinus cavities. OP0101 foam otic was the initial product candidate utilizing the foam platform. It was developed as an improved treatment option for acute otitis externa ("AOE"), a common infectious medical condition of the outer ear canal that affects tens of millions of adults and children each year (frequently called "swimmer's ear"). Novus completed four clinical trials of OP0101 foam otic in 353 adult and pediatric subjects, including a successful phase 2b study with a steroid-free, antibiotic-only formulation of OP0101 foam otic that was non-inferior to standard of care, but with a more favorable dosing regimen (once a day dosing instead of twice a day).OP0102 foam otic is a second-generation formulation designed to rapidly relieve ear pain (an unmet need in AOE) and eradicate infection with less than seven days of treatment. In May 2017, Novus suspended the foam otic platform development program to focus resources on the surfactant program.

RECENT DEVELOPMENTS

Equity Distribution Agreement

On July 23, 2018, the Company filed a prospectus supplement (the "2018 Prospectus") under which the Company may offer and sell, from time to time, through Piper Jaffray, up to an additional $9.8 million in shares of its common stock. Through December 31, 2019, Piper Jaffray has sold 25,218 shares of the Company's common stock under the 2018 Prospectus. As of December 31, 2019, $8.7 million of the $9.8 million shares of common stock remains available to be offered and sold under the 2018 Prospectus.

2019 Equity Offering

On April 30, 2019, the Company agreed to sell in a registered direct offering, an aggregate 3,449,112 shares of its common stock to certain investors for gross proceeds of approximately $10.7 million under its effective shelf registration statement on Form S-3 (File No. 333-226286). In a concurrent private placement, the Company also agreed to issue to such investors Series A warrants to purchase up to 3,449,112 shares of its common stock at an exercise price of $4.00 with a term of eighteen months and Series B warrants to purchase up 3,449,112 shares of its common stock at an exercise price of $4.00 with a term of five years. The Series B warrants become exercisable only upon the exercise of the Series A warrants. In addition, the Company agreed to issue to H.C. Wainwright & Co., LLC, the placement agent for the transaction, warrants to purchase up to 172,456 shares of common stock. The placement agent warrants have substantially the same terms as the Series A Warrants, except that the placement agent warrants have an exercise price equal to $3.86875 and will expire on April 20, 2014. We refer to the registered direct offering and the concurrent private placement collectively as the "2019 Equity Offering."

CRITICAL ACCOUNTING POLICIES AND SIGNIFICANT JUDGMENTS AND ESTIMATES

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States ("GAAP"). The preparation of these financial statements requires us to make estimates and judgments that affect the reported amount of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities as of the date of the financial statements. On an ongoing basis, we evaluate our estimates and judgments. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ materially from these estimates under different assumptions or conditions.

Goodwill

Goodwill represents the difference between the consideration transferred and the fair value of the net assets acquired under the acquisition method of accounting. Goodwill is not amortized but is evaluated for impairment as of October 1 of each year or earlier if indicators of impairment exist that would, more likely than not, reduce the fair value from its carrying amount.

The Company performs its goodwill impairment analysis at the reporting unit level, which aligns with the Company's reporting structure and availability of discrete financial information. The Company performs its annual impairment analysis by either comparing the reporting unit's estimated fair value to its carrying amount or doing a qualitative assessment of a reporting unit's fair value from the last quantitative assessment to determine if there is potential impairment. The Company may do a qualitative assessment when the results of the previous quantitative test indicated the reporting unit's estimated fair value was significantly in excess of the carrying value of its net assets and it does not believe there have been significant changes in the reporting unit's operations that would significantly decrease its estimated fair value or significantly increase its net assets. If a quantitative assessment is performed the evaluation includes management estimates of cash flow projections based on internal future projections and/or use of a market approach by looking at market values of comparable companies. Key assumptions for these projections include revenue growth, future gross and operating margin growth, and its weighted cost of capital and terminal growth rates. The revenue and margin growth are based on increased sales of new products as the Company maintains investments in research and development. Additional assumed value creators may include increased efficiencies from capital spending. The resulting cash flows are discounted using a weighted average cost of capital. Operating mechanisms and requirements to ensure that growth and efficiency assumptions will ultimately be realized are also considered in the evaluation, including timing and probability of regulatory approvals for Company products to be commercialized. The Company's market capitalization is also considered as a part of its analysis.

Research and Development Expenses

Research and development expenses include personnel and facility-related expenses, outside contracted services including clinical trial costs, manufacturing and process development costs, research costs and other consulting services and non-cash stock-based compensation. Research and development costs are expensed as incurred. Amounts due under contracts with third parties may be either fixed fee or fee for service, and may include upfront payments, monthly payments and payments upon the completion of milestones or receipt of deliverables. Non-refundable advance payments under agreements are capitalized and expensed as the related goods are delivered or services are performed.

The Company's contracts with third parties to perform various clinical trial activities in the on-going development of potential products. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows to its vendors. Payments under the contracts depend on factors such as the achievement of certain events, successful enrollment of patients, and completion of portions of the clinical trial or similar conditions. The Company's accrual for clinical trials is based on estimates of the services received and efforts expended pursuant to contracts with clinical trial centers and clinical research organizations. These contracts may be terminated by the Company upon written notice and the Company is generally only liable for actual effort expended by the organizations to the date of termination, although in certain instances the Company may be further responsible for termination fees and penalties. The Company estimates its research and development expenses and the related accrual as of each balance sheet date based on the facts and circumstances known to the Company at that time. There have been no material adjustments to the Company's prior period accrued estimates for clinical trial activities through December 31, 2019.

Stock-based Compensation

For stock options granted to employees, the Company recognizes compensation expense for all stock-based awards based on the grant-date estimated fair value. The fair value of stock options is determined using the Black-Scholes option pricing model, using assumptions which are subjective and require significant judgment and estimation by management. The risk-free rate assumption was based on observed yields from governmental zero-coupon bonds with an equivalent term. The expected volatility assumption was based on historical volatilities of a group of comparable industry companies whose share prices are publicly available. The peer group was developed based on companies in the pharmaceutical industry. The expected term of stock options represents the weighted-average period that the stock options are expected to be outstanding. Because the Company does not have historical exercise behavior, it determined the expected life assumption using the simplified method, which is an average of the options ordinary vesting period and the contractual term. The expected dividend assumption was based on the Company's history and expectation of dividend payouts. The Company has not paid and does not expect to pay dividends at any time in the foreseeable future. The Company recognizes forfeitures on an actual basis and as such did not estimate forfeitures to calculate stock-based compensation.

Restricted Stock Units ("RSU") and Performance-Based Restricted Stock Units ("PRSU") are measured and recognized based on the quoted market price of our common stock on the date of grant.

Stock-based compensation expense related to stock options granted to nonemployees is recognized based on the estimated fair value of the stock options on their grant date, determined using the Black-Scholes option pricing model. The awards generally vest over the period the Company expects to receive services from the nonemployees. Similar to stock options granted to employees, the fair value of stock options granted nonemployees, determined using the Black-Scholes option pricing model, involves assumptions that are subjective and require significant judgment and estimation by management. The risk-free rate assumption was based on observed yields from governmental zero-coupon bonds with an equivalent term. The expected volatility assumption was based on historical volatilities of a group of comparable industry companies whose share prices are publicly available. The peer group was developed based on companies in the pharmaceutical industry. The expected term of stock options represents the weighted-average period that the stock options are expected to be outstanding. Because the Company does not have historical exercise behavior on stock options granted to nonemployees, the Company determined the contractual term is the appropriate periods for expected life on stock options granted to nonemployees. The expected dividend assumption was based on the Company's history and expectation of dividend payouts. The Company has not paid and does not expect to pay dividends at any time in the foreseeable future. The Company recognizes forfeitures on an actual basis and as such did not estimate forfeitures to calculate stock-based compensation.

RESULTS OF OPERATIONS

Comparison of the Years Ended December 31, 2019 and 2018

The following table provides comparative results of operations for the years ended December 31, 2019 and 2018 (in thousands):

	Year Ended December 31,			
	2019	2018	$ Variance	% Variance
Operating expenses:				
Research and development	$ 8,128	$ 6,817	$ 1,311	19%
General and administrative	6,056	7,243	(1,187)	-16%
Goodwill impairment	1,867	-	1,867	100%
Total operating expenses	16,051	14,060	1,991	14%
Loss from operations	(16,051)	(14,060)	(1,991)	14%
Other income (expense), net	40	(5)	45	-900%
Net loss and other comprehensive loss	$ (16,011)	$ (14,065)	$ (1,946)	14%

Research and Development Expenses

The increase in research and development expenses of $1.3 million for the year ended December 31, 2019 was primarily due to an increase in clinical development costs of $1.8 million and an increase in consulting costs of $131,000 related to the advancement of our OP0201 programs, as well as an increase in stock-based compensation of $94,000. The increases were offset by a decrease in formulation and device development costs of $474,000, and decreases in personnel and travel related costs of $163,000 and $112,000, respectively. If the Company has a successful Phase 2a clinical study and we advance our clinical development programs, research and development expenses are expected to increase.

General and Administrative Expenses

The decrease in general and administrative expenses of $1.2 million for the year ended December 31, 2019 was primarily due to a reduction of $590,000 in administrative costs associated with operating a public company, as well as decreases in personnel costs and stock-based compensation of $163,000 and $330,000, respectively. Additionally, general operating costs decreased $87,000 and travel related expenses decreased $21,000. The decreases were offset by an increase in litigation costs of $4,000.

Goodwill Impairment

The Company performed a goodwill impairment test as of December 31, 2019 and determined that the fair value of its goodwill was below its carrying value. As a result, the Company recognized $1.9 million of goodwill impairment. No impairment was recorded for the year ended December 31, 2018.

Other Income (Expense), Net

The change in other income, net was due to an increase in interest income of $66,000, offset by an increase in realized losses on foreign currency translation of $19,000, and an increase in VAT tax of $2,000 for the year ended December 31, 2019.

LIQUIDITY AND CAPITAL RESOURCES

As of December 31, 2019, we had cash and cash equivalents of approximately $8.8 million, consisting of readily available cash in bank accounts and an accumulated deficit of $57.6 million. While we believe our cash and cash equivalents are not subject to excessive risk, we maintain significant amounts of cash and cash equivalents at one or more financial institutions that are in excess of federally insured limits. To date, our operations have been financed primarily by net proceeds from the sale of preferred and common stock and warrants, the issuance of convertible promissory notes, and cash received in a reverse merger with Tokai Pharmaceuticals, Inc. We have concluded and disclosed in the footnotes to our consolidated financial statements, included elsewhere within this Annual Report on Form 10-K, that we do not have sufficient cash to fund our operations through 12 months from the date of issuance of the most recent financial statements.

We do not have any approved products for commercial sale and have never generated revenue from product sales, and have incurred significant net losses since our inception and expect to continue to incur net operating losses for the foreseeable future. We do not expect to receive any revenue from any product candidates that we develop unless and until we obtain regulatory approval and commercialize our product candidates, or enter into collaborative arrangements with third parties. Our primary use of cash is to fund operating expenses, which consist of research and development expenses and general and administrative expenses. Cash used to fund operating expenses is impacted by the timing of when we pay or prepay these expenses. We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution.

We will continue to require additional financing in order to advance our surfactant drug product through clinical development, to manufacture, obtain regulatory approval for and to commercialize our product candidates, to develop, acquire or in-license other potential product candidates, and to fund operations for the foreseeable future. Therefore, we will seek to raise additional capital through equity offerings, debt financings or other capital sources, including potentially collaborations, licenses and other similar arrangements. Adequate additional funding may not be available to us on acceptable terms on a timely basis, or at all. Any such failure to raise capital as and when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies, and may cause us to delay the scope of or suspend one or more of our clinical trials, research and development programs or commercialization efforts, out-license intellectual property rights to our product candidates or sell unsecured assets, or a combination of the above. Any of these actions could materially harm our business. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. Debt financing, if available, would result in fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business. If we raise funds through collaborations, licenses and other similar arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. See the section of this Annual Report titled "Risk Factors" for additional risks associated with our substantial capital requirements and the challenges we may face in raising capital.

We plan to continue to fund losses from operations and capital funding needs through cash on hand and future equity or debt financings, as well as potential additional collaborations or strategic partnerships with other companies. During the third quarter of 2017, we entered into an equity distribution agreement pursuant to which we may sell shares of common stock from time to time in "at-the-market" offerings and filed a related prospectus supplement (the "2017 Prospectus"). On July 23, 2018, the Company filed the 2018 Prospectus. Under the 2017 Prospectus, we sold shares of common stock from October 2, 2017 through March 9, 2018 for gross proceeds of approximately $8.5 million. Under the 2018 Prospectus, we may offer and sell up to an additional $9.8 million in shares of common stock. Through December 31, 2019, we have sold 25,218 shares of the Company's common stock under the 2018 Prospectus for gross proceeds of approximately $110,000. As of December 31, 2019, $8.7 million of the $9.8 million shares of common stock remains available to be offered and sold under the 2018 Prospectus.

On April 30, 2019, the Company agreed to sell in a registered direct offering, an aggregate 3,449,112 shares of its common stock to certain investors for gross proceeds of approximately $10.7 million under its effective shelf registration statement on Form S-3 (File No. 333-226286). In a concurrent private placement, the Company also agreed to issue to such investors Series A warrants to purchase up to 3,449,112 shares of its common stock at an exercise price of $4.00 with a term of eighteen months and Series B warrants to purchase up 3,449,112 shares of its common stock at an exercise price of $4.00 with a term of five years. The Series B warrants become exercisable only upon the exercise of the Series A warrants. In addition, the Company agreed to issue to H.C. Wainwright & Co., LLC, the placement agent for the transaction, warrants to purchase up to 172,456 shares of common stock. The placement agent warrants have substantially the same terms as the Series A Warrants, except that the placement agent warrants have an exercise price equal to $3.86875 and will and will expire on April 30, 2024. We refer to the registered direct offering and the concurrent private placement collectively as the "2019 Equity Offering".

Our primary uses of capital are, and we expect will continue to be, funding research efforts and the development of our product candidates, compensation and related expenses, hiring additional staff (including clinical, scientific, operational, financial, and management personnel) and costs associated with operating as a public company. We expect to incur substantial expenditures in the foreseeable future for the development and potential commercialization of our product candidates.

On August 8, 2019, the Company received written notice (the "Notification Letter") from The Nasdaq Stock Market LLC ("Nasdaq") notifying the Company that it was not in compliance with the minimum bid price requirements set forth in Nasdaq Listing Rule 5550(a)(2) for continued listing on the Nasdaq Capital Market. Nasdaq Listing Rule 5550(a)(2) requires listed securities maintain a minimum closing bid price of $1.00 per share, and Nasdaq Listing Rule 5810(c)(3)(A) provides that a failure to meet the minimum closing bid price requirement exists if the deficiency continues for a period of 30 consecutive business days. Based on the closing bid price of the Company's common stock for the 30 consecutive business days prior to the date of the Notification Letter, the Company did not meet the minimum closing bid price requirement.

On February 6, 2020, the Company received written notice that Nasdaq determined that it is eligible for an additional 180-day extension (the "Extension Letter"), or until August 3, 2020, to regain compliance with the minimum bid price requirement. The Extension Letter does not impact the Company's listing on the Nasdaq Capital Market at this time. To regain compliance, the closing bid price of the Company's common stock must be at least $1.00 per share for a minimum of 10 consecutive business days at any time prior to August 3, 2020.

The Company intends to monitor the closing bid price of its common stock and consider its available options to resolve its noncompliance with the minimum bid price requirement. There can be no assurance that the Company will be able to regain compliance with the minimum bid price requirement or that the Company will otherwise be in compliance with other Nasdaq listing criteria. If the Company fails to regain compliance with the minimum bid requirement or to meet the other applicable continued listing requirements for the Nasdaq Capital Market in the future and Nasdaq determines to delist its common stock, the delisting could adversely affect the market price and liquidity of the Company's common stock and reduce its ability to raise additional capital.

If the Company's common stock is delisted by Nasdaq, the common stock may be eligible to trade on the OTC Bulletin Board or another over-the-counter market. Any such alternative would likely result in it being more difficult for the Company to raise additional capital through the public or private sale of equity securities and for investors to dispose of, or obtain accurate quotations as to the market value of, the common stock and could result in a decrease in the trading price of the common stock. In addition, there can be no assurance that the common stock would be eligible for trading on any such alternative exchange or markets.

As a result of these conditions, we have concluded that substantial doubt about our ability to continue as a going concern exists as conditions and events, considered in the aggregate, indicate that it is probable that we will be unable to meet our obligations as they become due within one year after the date that our consolidated financial statements were issued without raising additional capital. The financial information and consolidated financial statements included in this Annual Report have been prepared on a basis that assumes that we will continue as a going concern, which contemplates the realization of assets and the satisfaction of liabilities and commitments in the normal course of business. This financial information and these financial statements do not include any adjustments that may result from an unfavorable outcome of this uncertainty. Our ability to continue as a going concern is dependent upon our ability to successfully secure sources of financing and ultimately achieve profitable operations.

Cash Flows

The following table provides a summary of our net cash flow activity for the years ended December 31, 2019 and 2018 (in thousands):

	Year Ended December 31,	
	2019	2018
Net cash used in operating activities	$ (13,857)	$ (11,893)
Net cash provided by financing activities	9,676	7,562
Net decrease in cash, cash equivalents, and restricted cash	$ (4,181)	$ (4,331)

Comparison of the Years Ended December 31, 2019 and 2018

Net cash used in operating activities for the year ended December 31, 2019 consisted primarily of our net loss of $16.0 million, partially offset by non-cash items consisting primarily of depreciation and amortization of $182,000, a goodwill impairment charge of $1.9 million, and stock-based compensation totaling $1.3 million. Additionally, cash used in operating activities for the year ended December 31, 2019 reflected a net decrease in cash from changes in operating assets and liabilities of $1.2 million, due to a decrease in our accounts payable and accrued liabilities of $1.4 million and a decrease in our operating lease liability of $165,000, offset by a decrease in prepaid expenses and other assets of $354,000.

Net cash used in operating activities for the year ended December 31, 2018 consisted primarily of our net loss of $14.1 million, partially offset by non-cash items consisting primarily of depreciation and stock-based compensation totaling $1.6 million. Additionally, cash used in operating activities for the year ended December 31, 2018 reflected a net increase in cash from changes in operating assets and liabilities of $618,000, primarily due to an increase in our accounts payable and accrued liabilities.

There was no cash provided by or used in investing activities for the years ended December 31, 2019 and 2018.

Net cash provided by financing activities for the year ended December 31, 2019 was comprised of $9.6 million in net proceeds from the 2019 Equity Offering for the sale of approximately 3.4 million shares of common stock and $107,000 in net proceeds from the 2018 Prospectus for the sale of approximately 25,000 shares of common stock.

Net cash provided by financing activities for the year ended December 31, 2018 was comprised of net proceeds of $7.5 million from the issuance of approximately 2.3 million shares of common stock under the Equity Distribution Agreement, and proceeds from the exercise of stock options in the amount of $71,000.

Contractual Obligations

Contractual obligations represent future cash commitments and liabilities under agreements with third parties and exclude contingent liabilities for which we cannot reasonably predict future payment. Our contractual obligations primarily result from property leases for office space. Although we do have obligations for CRO services, the table below excludes potential payments we may be required to make under our agreements with CROs because timing of payments and actual amounts paid under those agreements may be different depending on the timing of receipt of goods or services or changes to agreed-upon terms or amounts for some obligations, and those agreements are cancelable upon written notice by the Company and therefore, not long-term liabilities. Additionally, the expected timing of payment of the obligations presented below is estimated based on current information.

The following table represents our contractual obligations as of December 31, 2019, aggregated by type (in thousands):

	Payments Due by Period				
Contractual Obligations	Total	Less than 1 year	1 - 3 years	3 - 5 years	More than 5 years
Operating Lease Obligations	$ 334	$ 188	$ 146	$ —	$ —
Total	$ 334	$ 188	$ 146	$ —	$ —

See *Note 5. Commitments and Contingencies* in the notes to the consolidated financial statements for a summary of contracts held by the Company as of December 31, 2019.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements as defined in the rules and regulations of the SEC.

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

Per §229.305 of Regulation S-K, the Company, designated a Smaller Reporting Company as defined in §229.10(f)(1) of Regulation S-K, is not required to provide the disclosure required by this Item.

Item 8. Financial Statements and Supplementary Data.

The Report of Independent Registered Public Accounting Firm, our consolidated financial statements and accompanying notes listed under Part IV, Item 15. *Exhibits, Financial Statement Schedules* of this Annual Report on Form 10-K are set forth beginning on page F-1 immediately following the signature page hereof and incorporated by reference herein.

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

Not applicable

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

As of December 31, 2019, our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the Company’s management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost benefit relationship of possible controls and procedures. Based on this evaluation, management concluded that our disclosure controls and procedures were effective in alerting them in a timely manner to material information required to be disclosed in our periodic reports filed with the SEC.

Internal Control Over Financial Reporting

Management’s Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rule 13a-15(f) under the Exchange Act. Our internal control system is designed to provide reasonable assurance to our management and board of directors regarding the preparation and fair presentation of published financial statements. All internal control systems, no matter how well designed, have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation.

Our management has assessed the effectiveness of our internal control over financial reporting as of December 31, 2019. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO Framework") in its 2013 *Internal Control—Integrated Framework.* Management believes that the COSO Framework is a suitable framework for its evaluation of financial reporting because it is free from bias, permits reasonably consistent qualitative and quantitative measurements of our internal control over financial reporting, is sufficiently complete so that those relevant factors that would alter a conclusion about the effectiveness of our internal control over financial reporting are not omitted and is relevant to an evaluation of internal control over financial reporting.

Based on this assessment, our management has concluded that as of December 31, 2019, our internal control over financial reporting is effective.

As a non-accelerated filer, we are not required to provide an attestation report on our internal control over financial reporting issued by the Company's independent registered accounting firm.

Changes in Internal Control over Financial Reporting

There have been no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) or 15d-15(f) of the Exchange Act) during the quarter ended December 31, 2019 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this Item 10 is incorporated herein by reference to information in our proxy statement for our 2020 Annual Meeting of Stockholders (the "2020 Proxy Statement"), which we expect to be filed with the SEC within 120 days of the end of our fiscal year ended December 31, 2019, including under headings "Board of Directors and Corporate Governance—Election of Directors," "Executive Officers and Executive Compensation—Executive Officers," "Board of Directors and Corporate Governance—Code of Business Conduct and Ethics," "Board of Directors and Corporate Governance—Director Nomination Process" and "Board of Directors and Corporate Governance—Committees of the Board of Directors".

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A copy of the code is available on the Corporate Governance section of our website, which is located at *http://ir.novustherapeutics.com/corporate-governance/governance-overview*. We intend to disclose on our website any amendments to, or waivers from, the code of business conduct and ethics that are required to be disclosed pursuant to the disclosure requirements of Item 5.05 of Form 8-K within four business days following the date of the amendment or waiver.

Item 11. Executive Compensation.

The information required by this Item 11 is incorporated herein by reference to information in our 2020 Proxy Statement, including under headings "Executive Compensation," "Director Compensation," "Board of Directors and Corporate Governance—Compensation Committee Interlocks and Insider Participation," "Board of Directors and Corporate Governance—Oversight of Risk".

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

The information required by this Item 12 is incorporated herein by reference to information in our 2020 Proxy Statement, including under headings "Security Ownership of Certain Beneficial Owners and Management" and "Securities Authorized for Issuance Under Equity Compensation Plans".

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

The information required by this Item 13 is incorporated herein by reference to information in our 2020 Proxy Statement, including under headings "Board of Directors and Corporate Governance—Related Person Transactions," "Board of Directors and Corporate Governance," and "Board of Directors and Corporate Governance—Committees of the Board of Directors".

Item 14. Principal Accounting Fees and Services.

The information required by this Item 14 is incorporated herein by reference to information in our 2020 Proxy Statement, including under headings "Proposal No. 2—Ratification of the Appointment of Independent Registered Public Accounting Firm".

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) The following documents are filed as part of this Annual Report on Form 10-K:

(1) Financial Statements:

The Report of Independent Registered Public Accounting Firm, our consolidated financial statements and accompanying notes are set forth beginning on page F-1 immediately following the signature page of this Annual Report on Form 10-K.

(2) Financial Statement Schedules:

The financial statement schedules are omitted as they are either not applicable or the information required is presented in the financial statements and notes thereto under Part II, Item 8. *Financial Statements and Supplementary Data*.

(3) Exhibits:

Exhibit Number	Exhibit Description	Incorporated by Reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
2.1	Amended and Restated Share Purchase Agreement dated as of March 2, 2017, by and among the Registrant, Otic Pharma, Ltd., and shareholders of Otic Pharma, Ltd., named therein.	10-K	001-36620	2.1	March 3, 2017	
3.1	Restated Certificate of Incorporation of Novus Therapeutics, Inc., a Delaware corporation, dated September 22, 2014	8-K	001-36620	3.1	September 26, 2014	
3.2	Certificate of Amendment to Certificate of Incorporation of Novus Therapeutics, Inc. (effecting, among other things a reverse stock-split), filed with the Secretary of the State of Delaware on May 9, 2017	8-K	001-36620	3.1	May 15, 2017	
3.3	Certificate of Amendment to Certificate of Incorporation of Novus Therapeutics, Inc. (effecting, among other things a change in the corporation's name to "Novus Therapeutics, Inc."), filed with the Secretary of the State of Delaware on May 9, 2017	8-K	001-36620	3.2	May 15, 2017	
3.4	Amended and Restated Bylaws of Novus Therapeutics, Inc.	8-A/A	001-36620	3.4	June 23, 2017	
4.1	Form of Common Stock Certificate	8-A/A	001-36620	4.1	June 23, 2017	
4.2	Form of Warrant	8-K	001-36620	4.1	May 2, 2019	
4.3	Form of Placement Agent Warrant	8-K	001-36620	4.2	May 2, 2019	
4.4	Description of Securities					X
10.1	Registration Rights Agreement, dated May 10, 2017, by and among the Company and the Purchasers	8-K	001-36620	10.1	May 15, 2017	
10.2*	Form of Indemnification Agreement between Novus Therapeutics, Inc. and each of its directors and executive officers	10-Q	001-36620	10.1	August 9, 2017	

Exhibit Number	Exhibit Description	Incorporated by Reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
10.3	Lease Agreement, dated as of September 2, 2015, by and between The Irvine Company LLC and Otic Pharma, Inc.	10-Q	001-36620	10.2	August 9, 2017	
10.4	First Amendment to Lease Agreement, dated April 19, 2018, by and between The Irvine Company LLC and Novus Therapeutics, Inc.	10-Q	001-36620	10.1	August 7, 2018	
10.5*	Executive Employment Agreement, dated July 15, 2015, between Otic Pharma, Inc., and Gregory J. Flesher	10-Q	001-36620	10.3	August 9, 2017	
10.6	Exclusive License Agreement, dated November 1, 2015, between Scientific Development and Research, Inc. and Otodyne, Inc., on the one hand, and Oticpharma, Inc., on the other hand†	10-Q	001-36620	10.4	August 9, 2017	
10.7*	Offer of Employment, dated July 1, 2017, from Novus Therapeutics, Inc. to Jon Kuwahara	10-Q	001-36620	10.5	August 9, 2017	
10.8*	Management Continuity Agreement, dated August 7, 2017, between Novus Therapeutics, Inc. and Gregory J. Flesher	10-Q	001-36620	10.6	August 9, 2017	
10.9*	Management Continuity Agreement, dated August 7, 2017, between Novus Therapeutics, Inc. and Jon S. Kuwahara	10-Q	001-36620	10.7	August 9, 2017	
10.10	Equity Distribution Agreement, dated as of August 21, 2017, between Novus Therapeutics, Inc. and Piper Jaffray & Co.	8-K	001-36620	1.1	August 22, 2017	
10.11	Otic Pharma Ltd. Global Share Incentive Plan (2012)	10-K	001-36620	10.10	April 2, 2018	
10.12	Tokai Pharmaceuticals, Inc. 2007 Stock Incentive Plan	10-K	001-36620	10.11	April 2, 2018	
10.13	Tokai Pharmaceuticals, Inc. 2014 Stock Incentive Plan	10-Q	001-36620	10.2	August 7, 2018	
10.14	Novus Therapeutics, Inc., 2014 Employee Stock Purchase Plan	10-Q	001-36620	10.3	August 7, 2018	
10.15*	Executive Employment Agreement, dated November 10, 2015, between Otic Pharma, Inc. and Catherine C. Turkel	10-K	001-36620	10.15	March 27, 2019	
10.16*	Management Continuity Agreement, date August 7, 2017, between Novus Therapeutics, Inc. and Catherine C. Turkel	10-Q	001-36620	10.1	May 14, 2019	
10.17	Form of Securities Purchase Agreement, dated April 30, 2019, by and between Novus Therapeutics, Inc. and the Purchasers named therein	8-K	001-36620	10.1	May 2, 2019	
16.1	.Letter from Ernst & Young LLP, dated July 11, 2019	8-K	001-36620	16.1	July 12, 2019	
21.1	Subsidiaries of the Registrant					X

Exhibit Number	Exhibit Description	Incorporated by Reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
23.1	Consent of Ernst & Young LLP, independent registered public accounting firm					X
23.2	Consent of KMJ Corbin & Company LLP, independent registered public accounting firm					X
31.1	. Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
32.1#	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
32.2#	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
101.INS	XBRL Instance Document					
101.SCH	XBRL Taxonomy Extension Schema Document					
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document					
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document					
101.LAB	XBRL Taxonomy Extension Label Linkbase Document					
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document					
*	Indicates a management contract or compensatory plan					
†	Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission pursuant to a request for confidential treatment.					
#	These certifications are not deemed filed by the SEC and are not to be incorporated by reference in any filing we make under the Securities Act of 1933 or the Securities Exchange Act of 1934, irrespective of any general incorporation language in any filings.					

Item 16. Form 10-K Summary.

None.

SIGNATURES

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

Novus Therapeutics, Inc.

Date: March 16, 2020 By: /s/ Gregory J. Flesher

Gregory J. Flesher
Chief Executive Officer and Director (Principal Executive Officer)

Date: March 16, 2020 By: /s/ Jon S. Kuwahara

Jon S. Kuwahara
Senior Vice President Finance & Administration (Principal Financial and Accounting Officer)

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/ Gregory J. Flesher **Gregory J. Flesher**	Chief Executive Officer and Director **(**Principal Executive Officer)	March 16, 2020
/s/ Jon S. Kuwahara **Jon S. Kuwahara**	Senior Vice President Finance & Administration (Principal Financial and Accounting Officer)	March 16, 2020
/s/ Keith A. Katkin **Keith A. Katkin**	Chairman of the Board of Directors	March 16, 2020
/s/ Erez Chimovits **Erez Chimovits**	Director	March 16, 2020
/s/ Cheryl L. Cohen **Cheryl L. Cohen**	Director	March 16, 2020
/s/ Gary A. Lyons **Gary A. Lyons**	Director	March 16, 2020
/s/ John S. McBride **John S. McBride**	Director	March 16, 2020

NOVUS THERAPEUTICS, INC.
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Novus Therapeutics, Inc.

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheet of Novus Therapeutics, Inc. (the "Company") as of December 31, 2019, the related consolidated statement of operations and comprehensive loss, stockholders' equity and cash flows for the year ended December 31, 2019, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2019, and the results of its operations and its cash flows for the year ended December 31, 2019, in conformity with accounting principles generally accepted in the United States of America.

Going Concern

The accompanying consolidated financial statements have been prepared assuming the Company will continue as a going concern. As discussed in Note 2 to the consolidated financial statements, the Company has experienced recurring losses and negative cash flows from operations since inception, has an accumulated deficit of approximately $57.6 million as of December 31, 2019 and is dependent on its ability to raise capital. These factors raise substantial doubt about the Company's ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 2. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audit. We 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 audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audit we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audit 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 audit 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. We believe that our audit provides a reasonable basis for our opinion.

/s/ KMJ Corbin & Company LLP

We have served as the Company's auditor since 2019.

Irvine, California
March 16, 2020

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Novus Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheet of Novus Therapeutics, Inc. (the Company) as of December 31, 2018, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for the year ended December 31, 2018, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2018, and the results of its operations and its cash flows for the year ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

The Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 2 to the financial statements, the Company has suffered recurring losses and negative cash flows from operations since inception and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 2. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audit. 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 audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audit we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audit included performing procedures to assess the risks of material misstatement of the 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 financial statements. Our audit also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audit provides a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We served as the Company's auditor from 2017 to 2019.

Irvine, California
March 27, 2019

NOVUS THERAPEUTICS, INC.
CONSOLIDATED BALANCE SHEETS
(In thousands, except share data)

	December 31, 2019	December 31, 2018
ASSETS		
Current assets:		
Cash and cash equivalents	$ 8,791	$ 12,972
Prepaid expenses and other current assets	1,180	1,304
Total current assets	9,971	14,276
Property and equipment, net	5	14
Operating lease asset, net	316	—
Goodwill	—	1,867
Other assets	639	869
Total assets	$ 10,931	$ 17,026
LIABILITIES AND STOCKHOLDERS' EQUITY		
Accounts payable	$ 329	$ 689
Current operating lease liability	180	—
Accrued expenses and other liabilities	813	1,845
Total current liabilities	1,322	2,534
Non-current operating lease liability	144	—
Total liabilities	1,466	2,534
Commitments and contingencies (Note 5)		
Stockholders' equity:		
Preferred stock, $0.001 par value, 5,000,000 shares authorized and none issued and outstanding at December 31, 2019 and 2018	—	—
Common stock, $0.001 par value, 200,000,000 shares authorized at December 31, 2019 and 2018; 12,967,338 and 9,422,143 shares issued and outstanding at December 31, 2019 and 2018, respectively	13	9
Additional paid-in capital	67,034	56,054
Accumulated deficit	(57,582)	(41,571)
Total stockholders' equity	9,465	14,492
Total liabilities and stockholders' equity	$ 10,931	$ 17,026

See accompanying notes to consolidated financial statements.

NOVUS THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except share and per share data)

	Year Ended December 31,	
	2019	2018
Operating expenses		
Research and development	$ 8,128	$ 6,817
General and administrative	6,056	7,243
Goodwill impairment	1,867	—
Total operating expenses	16,051	14,060
Loss from operations	(16,051)	(14,060)
Other income (expense), net	40	(5)
Net loss and other comprehensive loss	$ (16,011)	$ (14,065)
Net loss per share, basic and diluted	$ (1.36)	$ (1.56)
Weighted-average common shares outstanding, basic and diluted	11,799,468	9,005,352

See accompanying notes to consolidated financial statements.

NOVUS THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(In thousands, except share data)

	Stockholders' Equity				
	Common Stock				
	Shares	Amount	Additional Paid-In Capital	Accumulated Deficit	Total
Balance as of December 31, 2017	7,110,414	$ 7	$ 46,951	$ (27,506)	$ 19,452
Issuance of common stock at-the-market, net of issuance costs	2,296,610	2	7,489	—	7,491
Issuance of common stock in connection with exercise of options	15,119	—	71	—	71
Stock-based compensation	—	—	1,543	—	1,543
Net loss and other comprehensive loss	—	—	—	(14,065)	(14,065)
Balance as of December 31, 2018	9,422,143	9	56,054	(41,571)	14,492
Issuance of common stock at-the-market, net of issuance costs	25,218	—	107	—	107
Issuance of common stock and warrants in registered direct offering, net of issuance costs	3,449,112	4	9,565	—	9,569
Issuance of common stock in connection with vesting of restricted stock units	78,450	—	—	—	—
Cancellation of common stock	(7,585)	—	—	—	—
Stock-based compensation	—	—	1,308	—	1,308
Net loss and other comprehensive loss	—	—	—	(16,011)	(16,011)
Balance as of December 31, 2019	12,967,338	$ 13	$ 67,034	$ (57,582)	$ 9,465

See accompanying notes to consolidated financial statements.

NOVUS THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,	
	2019	**2018**
Operating activities		
Net loss	$ (16,011)	$ (14,065)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	9	11
Amortization of operating lease asset	173	
Goodwill impairment	1,867	—
Stock-based compensation	1,308	1,543
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	354	(476)
Accounts payable and accrued expenses	(1,392)	1,094
Operating lease liability	(165)	—
Net cash used in operating activities	(13,857)	(11,893)
Financing activities		
Proceeds from issuances of common stock, net	9,676	7,491
Proceeds from exercise of stock options	—	71
Net cash provided by financing activities	9,676	7,562
Net decrease in cash and cash equivalents	(4,181)	(4,331)
Cash and cash equivalents at beginning of year	12,972	17,303
Cash and cash equivalents at end of year	$ 8,791	$ 12,972

See accompanying notes to consolidated financial statements.

Note 1. Description of Business

Novus Therapeutics, Inc. is a specialty pharmaceutical company focused on developing products for disorders of the ear, nose, and throat. Unless otherwise indicated, references to the terms “Novus,” “our,” ‘us,” “we”, or the “Company” refer to Novus Therapeutics, Inc.

In 2017, Otic Pharma, Ltd. (“Otic”) consummated a reverse merger with Tokai Pharmaceuticals, Inc. (“Tokai”), pursuant to which, among other things, Tokai purchased from Otic and its stockholders all of the common and preferred shares of Otic in exchange for the issuance of a certain number of shares of common stock of Tokai (the “Reverse Merger”). Following the Reverse Merger, Tokai changed its name to Novus Therapeutics, Inc.

Note 2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The consolidated financial statements are prepared in accordance with accounting principles generally accepted in the United States (“GAAP”). Novus, a Delaware corporation, owns 100% of the issued and outstanding common stock or other ownership interest in Otic Pharma, Ltd., a private limited company organized under the laws of the State of Israel (“Otic”). Otic owns 100% of the issued and outstanding common stock or other ownership interest in its U.S. subsidiary, Otic Pharma, Inc. The functional currency of the Company’s foreign subsidiary is the U.S. Dollar; however, certain expenses, assets and liabilities are transacted at the local currency. These transactions are translated from the local currency into U.S. Dollars at exchange rates during or at the end of the reporting period. The activities of the Company’s foreign subsidiary are not significant to the consolidated financial statements.

All significant intercompany accounts and transactions among the entities have been eliminated in consolidation.

Liquidity and Financial Condition

The Company has experienced recurring net losses and negative cash flows from operating activities since its inception. The Company recorded a net loss of $16.0 million and used $13.9 million of cash in operating activities for the year ended December 31, 2019. As of December 31, 2019, the Company had cash and cash equivalents of $8.8 million, working capital of $8.6 million and an accumulated deficit of $57.6 million. Due to continuing research and development activities, the Company expects to continue to incur net losses into the foreseeable future. In order to continue these activities, the Company will need to raise additional funds through public or private debt and equity financings or strategic collaboration and licensing arrangements. The Company’s ability to raise additional capital in the equity and debt markets is dependent on a number of factors, including, but not limited to, the market demand for the Company’s common stock, which itself is subject to a number of development and business risks and uncertainties, as well as the uncertainty that the Company would be able to raise such additional capital at a price or on terms that are favorable to the Company. If the Company issues equity or convertible debt securities to raise additional funding, its existing stockholders may experience dilution, it may incur significant financing costs, and the new equity or convertible debt securities may have rights, preferences and privileges senior to those of its existing stockholders. If the Company issues debt securities to raise additional funding, it would incur additional debt service obligations, it could become subject to additional restrictions limiting its ability to operate its business, and it may be required to further encumber its assets.

Adequate additional funding may not be available to us on acceptable terms on a timely basis, or at all. During fiscal year 2019, the Company has implemented, and will continue to implement, certain cost cutting measures to reduce its cash flow requirements. Consistent with the actions the Company has taken in the past, it will execute the appropriate steps to enable the continued operation of the business and preservation of the value of its assets beyond the next twelve months, including but not limited to actions such as reduced personnel-related costs, delay or curtailment of the Company’s research and development activities, and other discretionary expenses that are within the Company’s control. These initiatives, if required, may have an adverse impact on the Company’s ability to achieve certain of its planned objectives as it seeks strategic alternatives.

On August 8, 2019, the Company received written notice (the "Notification Letter") from the Nasdaq Stock Market LLC ("Nasdaq") notifying the Company that it was not in compliance with the minimum bid price requirements set forth in Nasdaq Listing Rule 5550(a)(2) for continued listing on The Nasdaq Capital Market. Nasdaq Listing Rule 5550(a)(2) requires listed securities maintain a minimum closing bid price of $1.00 per share, and Nasdaq Listing Rule 5810(c)(3)(A) provides that a failure to meet the minimum closing bid price requirement exists if the deficiency continues for a period of 30 consecutive business days. Based on the closing bid price of the Company's common stock for the 30 consecutive business days prior to the date of the Notification Letter, the Company did not meet the minimum closing bid price requirement.

On February 6, 2020, the Company received written notice that Nasdaq determined that it is eligible for an additional 180-day extension (the "Extension Letter"), or until August 3, 2020, to regain compliance with the minimum bid price requirement. The Extension Letter does not impact the Company's listing on the Nasdaq Capital Market at this time. To regain compliance, the closing bid price of the Company's common stock must be at least $1.00 per share for a minimum of 10 consecutive business days at any time prior to August 3, 2020.

The Company intends to monitor the closing bid price of its common stock and consider its available options to resolve its noncompliance with the minimum bid price requirement. There can be no assurance that the Company will be able to regain compliance with the minimum bid price requirement or that the Company will otherwise be in compliance with other Nasdaq listing criteria. If the Company fails to regain compliance with the minimum bid requirement or to meet the other applicable continued listing requirements for the Nasdaq Capital Market in the future and Nasdaq determines to delist its common stock, the delisting could adversely affect the market price and liquidity of the Company's common stock and reduce its ability to raise additional capital.

If the Company's common stock is delisted by Nasdaq, the common stock may be eligible to trade on the OTC Bulletin Board or another over-the-counter market. Any such alternative would likely result in it being more difficult for the Company to raise additional capital through the public or private sale of equity securities and for investors to dispose of, or obtain accurate quotations as to the market value of, the common stock and could result in a decrease in the trading price of the common stock. In addition, there can be no assurance that the common stock would be eligible for trading on any such alternative exchange or markets.

At the time of issuance of the consolidated financial statements for the year ended December 31, 2019, the Company concluded that there is substantial doubt regarding the Company's ability to continue as a going concern for the twelve months from the date of issuance of the consolidated financial statements for the year ended December 31, 2019. The financial information and the consolidated financial statements included in this Annual Report have been prepared on a basis that assumes that we will continue as a going concern, which contemplates the realization of assets and the satisfaction of liabilities and commitments in the normal course of business. This financial information and these consolidated financial statements do not include any adjustments that may result from an unfavorable outcome of this uncertainty. Our ability to continue as a going concern is dependent upon our ability to successfully secure sources of financing and ultimately achieve profitable operations.

Use of Estimates

The preparation of the Company's consolidated financial statements in conformity with GAAP requires management to make informed estimates and assumptions that affect the reported amounts of assets, liabilities and expenses and the disclosure of contingent assets and liabilities in the Company's consolidated financial statements and accompanying notes. The most significant estimates in the Company's financial statements relate to stock-based compensation, accruals for liabilities, operating lease liability, carrying value of goodwill, and other matters that affect the consolidated financial statements and related disclosures. Actual results could differ materially from those estimates under different assumptions or conditions and the differences may be material to the consolidated financial statements.

Cash and Cash Equivalents

Cash represents cash deposits held at financial institutions. The Company considers all liquid investments purchased with an original maturity of three months or less and that can be liquidated without prior notice or penalty to be cash equivalents. The carrying value of cash equivalents approximates their fair value due to the short-term maturities of these instruments. Cash equivalents are held for the purpose of meeting short-term liquidity requirements, rather than for investment purposes. The Company had no cash equivalents at December 31, 2019 and 2018.

Fair Value Measurements

Financial assets and liabilities are recorded at fair value.

The Company measures the fair value of certain of its financial instruments on a recurring basis. A fair value hierarchy is used to rank the quality and reliability of the information used to determine fair values. Financial assets and liabilities carried at fair value will be classified and disclosed in one of the following three categories:

Level 1—Quoted prices (unadjusted) in active markets for identical assets and liabilities.

Level 2—Inputs other than Level 1 that are observable, either directly or indirectly, such as unadjusted quoted prices for similar assets and liabilities, unadjusted quoted prices in the markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

There have been no transfers of assets for liabilities between these fair value measurement classifications during the periods presented.

The Company had no financial instruments, assets or liabilities measured at fair value on a recurring basis at December 31, 2019 and 2018.

Concentration of Credit Risk and Other Risks and Uncertainties

As of December 31, 2019 and 2018, all of the Company's long-lived assets were located in the United States.

Financial instruments that are subject to concentration of credit risk consist primarily of cash equivalents. The Company's policy is to invest cash in institutional money market funds to limit the amount of credit exposure. At times, the Company maintains cash equivalents in short-term money market funds and it has not experienced any losses on its cash equivalents.

The Company's products will require approval from the U.S. Food and Drug Administration ("FDA") and foreign regulatory agencies before commercial sales can commence. There can be no assurance that its products will receive any of these required approvals. The denial or delay of such approvals may impact the Company's business in the future. In addition, after the approval by the FDA, there is still an ongoing risk of adverse events that did not appear during the product approval process.

The Company is subject to risks common to companies in the pharmaceutical industry, including, but not limited to, new technological innovations, clinical development risk, establishment of appropriate commercial partnerships, protection of proprietary technology, compliance with government and environmental regulations, uncertainty of market acceptance of products, product liability, the volatility of its stock price and the need to obtain additional financing.

Our facilities and equipment may be affected by natural or man-made disasters. We currently conduct our research, development and management activities in Irvine, California, near known earthquake fault zones. We have taken precautions to safeguard our facilities, equipment and systems, including insurance, health and safety protocols, and off-site storage of computer data. However, our facilities and systems may be vulnerable to earthquakes, fire, storm, power loss, telecommunications failures, physical and software break-ins, software viruses and similar events which could cause substantial delays in our operations, damage or destroy our equipment or inventory, and cause us to incur additional expenses. In addition, the insurance coverage we maintain may not be adequate to cover our losses in any circumstance and may not continue to be available to use on acceptable terms, or at all.

Reportable Segments

Operating segments under GAAP are defined as components of an enterprise about which separate financial information is available that is evaluated regularly by the Chief Operating Decision Maker ("CODM"), or decision-making group, in deciding how to allocate resources and in assessing performance. The CODM is the Company's Chief Executive Officer and the Company has determined that it operates in one business segment, which is the development of products for disorders of the ear, nose, and throat.

Goodwill

Goodwill represents the difference between the consideration transferred and the fair value of the net assets acquired under the acquisition method of accounting. Goodwill is not amortized but is evaluated for impairment as of October 1 of each year or if indicators of impairment exist that would, more likely than not, reduce the fair value from its carrying amount.

The Company performs its goodwill impairment analysis at the reporting unit level, which aligns with the Company's reporting structure and availability of discrete financial information. The Company performs its annual impairment analysis by either comparing the reporting unit's estimated fair value to its carrying amount or doing a qualitative assessment of a reporting unit's fair value from the last quantitative assessment to determine if there is potential impairment. The Company may do a qualitative assessment when the results of the previous quantitative test indicated the reporting unit's estimated fair value was significantly in excess of the carrying value of its net assets and it does not believe there have been significant changes in the reporting unit's operations that would significantly decrease its estimated fair value or significantly increase its net assets. If a quantitative assessment is performed the evaluation includes management estimates of cash flow projections based on internal future projections and/or use of a market approach by looking at market values of comparable companies. Key assumptions for these projections include revenue growth, future gross and operating margin growth, and its weighted cost of capital and terminal growth rates. The revenue and margin growth is based on increased sales of new products as the Company maintains investments in research and development. Additional assumed value creators may include increased efficiencies from capital spending. The resulting cash flows are discounted using a weighted average cost of capital. Operating mechanisms and requirements to ensure that growth and efficiency assumptions will ultimately be realized are also considered in the evaluation, including timing and probability of regulatory approvals for Company products to be commercialized. The Company's market capitalization is also considered as a part of its analysis.

The Company's annual evaluation for impairment of goodwill consists of one reporting unit. In accordance with the Company's policy, the Company completed its annual evaluation for impairment as of October 1, 2019 using the qualitative assessment and determined that no impairment existed. However, due to declining market conditions, the Company performed an additional goodwill impairment test as of December 31, 2019 and determined that the fair value of its goodwill was below its carrying value. As a result, the Company recognized $1.9 million of goodwill impairment which was included in the consolidated statements of operations. No impairment was recorded for the year ended December 31, 2018.

Long-Lived Assets

Property and equipment are recorded at cost. Depreciation is computed using the straight-line method over the estimated useful lives of the respective assets. Additions, major renewals and improvements are capitalized and repair and maintenance costs are charged to expense as incurred. Leasehold improvements are amortized over the remaining life of the initial lease term or the estimated useful lives of the assets, whichever is shorter.

The Company reviews property and equipment for impairment whenever events or changes in circumstances indicate that the carrying value of an asset may not be recoverable. An impairment loss would be recognized when estimated future undiscounted cash flows relating to the asset are less than its carrying amount. An impairment loss is measured as the amount by which the carrying amount of an asset exceeds its fair value. Significant management judgment is required in the forecast of future operating results that are used in the preparation of expected cash flows. No impairments of tangible assets have been identified during the years presented.

Research and Development Expenses

Research and development expenses include personnel and facility-related expenses, outside contracted services including clinical trial costs, manufacturing and process development costs, research costs and other consulting services and non-cash stock-based compensation. Research and development costs are expensed as incurred. Amounts due under contracts with third parties may be either fixed fee or fee for service, and may include upfront payments, monthly payments and payments upon the completion of milestones or receipt of deliverables. Non-refundable advance payments under agreements are capitalized and expensed as the related goods are delivered or services are performed.

The Company's contracts with third parties to perform various clinical trial activities in the on-going development of potential products. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows to its vendors. Payments under the contracts depend on factors such as the achievement of certain events, successful enrollment of patients, and completion of portions of the clinical trial or similar conditions. The Company's accrual for clinical trials is based on estimates of the services received and efforts expended pursuant to contracts with clinical trial centers and clinical research organizations. These contracts may be terminated by the Company upon

written notice and the Company is generally only liable for actual effort expended by the organizations to the date of termination, although in certain instances the Company may be further responsible for termination fees and penalties. The Company estimates its research and development expenses and the related accrual as of each balance sheet date based on the facts and circumstances known to the Company at that time. There have been no material adjustments to the Company's prior period accrued estimates for clinical trial activities through December 31, 2019.

Net Loss Per Share

Basic net loss per common share is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of common shares outstanding during the period, without consideration for potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders by the weighted-average number of common shares and potentially dilutive securities outstanding for the period determined using the treasury-stock and if-converted methods. For purposes of the diluted net loss per share calculation, preferred stock, and stock options and warrants are considered to be potentially dilutive securities and are excluded from the calculation of diluted net loss per share because their effect would be anti-dilutive. Therefore, basic and diluted net loss per share was the same for the periods presented due to the Company's net loss position.

	Year Ended December 31,	
	2019	2018
	(In thousands, except share and per share data)	
Net loss	$ (16,011)	$ (14,065)
Net loss per share, basic and diluted	$ (1.36)	$ (1.56)
Weighted-average number of common shares	11,799,468	9,005,352

The computation of diluted earnings per share excludes stock options, warrants, and restricted stock units that are anti-dilutive. For the year ended December 31, 2019, common share equivalents of 8,770,947 shares were anti-dilutive. For the year ended December 31, 2018, common share equivalents of 974,817 shares were anti-dilutive.

Stock-based Compensation

For stock options granted to employees, the Company recognizes compensation expense for all stock-based awards based on the grant-date estimated fair value. The fair value of stock options is determined using the Black-Scholes option pricing model, using assumptions which are subjective and require significant judgment and estimation by management. The risk-free rate assumption was based on observed yields from governmental zero-coupon bonds with an equivalent term. The expected volatility assumption was based on historical volatilities of a group of comparable industry companies whose share prices are publicly available. The peer group was developed based on companies in the pharmaceutical industry. The expected term of stock options represents the weighted-average period that the stock options are expected to be outstanding. Because the Company does not have historical exercise behavior, it determined the expected life assumption using the simplified method, which is an average of the options ordinary vesting period and the contractual term. The expected dividend assumption was based on the Company's history and expectation of dividend payouts. The Company has not paid and does not expect to pay dividends at any time in the foreseeable future. The Company recognizes forfeitures on an actual basis and as such did not estimate forfeitures to calculate stock-based compensation.

Restricted Stock Units ("RSU") and Performance-Based Restricted Stock Units ("PRSU") are measured and recognized based on the quoted market price of our common stock on the date of grant.

Effective as of August 1, 2018, the Board of Directors amended the Company's 2014 Stock Incentive Plan (the "2014 Plan") and the Company's 2014 Employee Stock Purchase Plan (the "ESPP" and, together with the 2014 Plan, the "Plans") to reduce the share reserves under the Plans. These reductions were made to equitably adjust the share reserves in accordance with the terms of the Plans. As a result of these equitable adjustments: (1) the number of shares of common stock authorized for issuance under the 2014 Plan (excluding shares underlying outstanding awards as of August 1, 2018) was reduced to 766,500 shares and the maximum number of shares that can be added to the 2014 Plan under the evergreen provision set forth in Section 4(a)(1)(C) of the 2014 Plan was reduced to 550,000 shares annually; and (2) the number of shares of common stock authorized for future issuance under the ESPP was reduced to 209,500 shares (excluding shares previously issued under the ESPP prior to August 1, 2018) and the maximum number of shares that can be added to the ESPP under the evergreen provision set forth in the ESPP was reduced to 135,000 shares annually. The 2014 Plan and ESPP were amended and restated

as of August 1, 2018 to reflect these equitable adjustments. The number of shares reserved for issuance under the 2014 Plan and ESPP were 337,955 and 303,721 shares, respectively, as of December 31, 2019

Stock-based compensation expense related to stock options granted to nonemployees is recognized based on the estimated fair value of the stock options on their grant date, determined using the Black-Scholes option pricing model. The awards generally vest over the period the Company expects to receive services from the nonemployees. Similar to stock options granted to employees, the fair value of stock options granted to nonemployees, is determined using the Black-Scholes option pricing model, involves assumptions that are subjective and require significant judgment and estimation by management. The risk-free rate assumption was based on observed yields from governmental zero-coupon bonds with an equivalent term. The expected volatility assumption was based on historical volatilities of a group of comparable industry companies whose share prices are publicly available. The peer group was developed based on companies in the pharmaceutical industry. The expected term of stock options represents the weighted-average period that the stock options are expected to be outstanding. Because the Company does not have historical exercise behavior on stock options granted to nonemployees, the Company determined the contractual term is the appropriate periods for expected life on stock options granted to nonemployees. The expected dividend assumption was based on the Company's history and expectation of dividend payouts. The Company has not paid and does not expect to pay dividends at any time in the foreseeable future. The Company recognizes forfeitures on an actual basis and as such did not estimate forfeitures to calculate stock-based compensation.

Income Taxes

The asset and liability approach is used to recognize deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the carrying amounts and the tax bases of assets and liabilities. Tax law and rate changes are reflected in income in the period such changes are enacted. The likelihood of realizing the tax benefits related to a potential deferred tax asset is evaluated, and a valuation allowance is recognized to reduce that deferred tax asset if it is more likely than not that all or some portion of the deferred tax asset will not be realized. Deferred tax assets and liabilities are calculated at the beginning and end of the year; the change in the sum of the deferred tax asset, valuation allowance and deferred tax liability during the year generally is recognized as a deferred tax expense or benefit. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in operations in the period that includes the enactment date.

Significant judgment is required in determining the Company's provision for income taxes, deferred tax assets and liabilities and the valuation allowance recorded against net deferred tax assets. We assess the likelihood that deferred tax assets will be recovered as deductions from future taxable income. The evaluation of the need for a valuation allowance is performed on a jurisdiction-by-jurisdiction basis and includes a review of all available positive and negative evidence. Factors reviewed include projections of pre-tax book income for the foreseeable future, determination of cumulative pre-tax book income after permanent differences, earnings history, and reliability of forecasting. We have provided a full valuation allowance on our deferred tax assets as of December 31, 2019 and 2018 because we believe it is more likely than not that our deferred tax assets will not be realized as of those dates.

The Company evaluates the accounting for uncertainty in income tax recognized in its consolidated financial statements and determines whether it is more likely than not that a tax position will be sustained upon examination by the appropriate taxing authorities before any part of the benefit is recorded in its consolidated financial statements. For those tax positions where it is "not more likely than not" that a tax benefit will be sustained, no tax benefit is recognized. Where applicable, associated interest and penalties are also recorded. The Company has not accrued any liabilities for any such uncertain tax positions as of December 31, 2019 and 2018. The Company is subject to U.S. federal and state tax authority examinations for all the years since inception due to net operating loss and tax credit carryforwards. The net operating losses and tax credits are subject to adjustment until the statute closes on the year the attributes are ultimately utilized.

The Company's income tax returns are based on calculations and assumptions that are subject to examination by the Internal Revenue Service and other tax authorities. In addition, the calculation of the Company's tax liabilities involves dealing with uncertainties in the application of complex tax regulations. The Company recognizes liabilities for uncertain tax positions based on a two-step process. The first step is to evaluate the tax position for recognition by determining if the weight of available evidence indicates that it is more likely than not that the position will be sustained on audit, including resolution of related appeals or processes, if any. The second step is to measure the tax benefit as the largest amount that is more than 50% likely of being realized upon settlement. While the Company believes it has appropriate support for the positions taken on its tax returns, the Company regularly assesses the potential outcomes of examinations by tax authorities in determining the adequacy of its provision for income taxes. The Company continually assesses the likelihood and amount of potential revisions and adjusts the income tax provision, income taxes payable and deferred taxes in the period in which the facts that give rise to a revision become known. For additional information, see *Note 7. Income Taxes* in the notes to the consolidated financial statements.

Recently Issued Accounting Pronouncements

In August 2018, the Financial Accounting Standards Board ("FASB") issued ASU 2018-15, *Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract* ("ASU 2018-15"), an amendment to the accounting guidance on cloud computing service arrangements that changes the accounting for implementation costs incurred in a cloud computing arrangement that is a service contract. The update aligns the requirements for capitalizing implementation costs incurred in a hosting arrangement that is a service contract with the requirements for capitalizing implementation costs incurred to develop or obtain internal-use software. The guidance also requires an entity to expense the capitalized implementation costs of a hosting arrangement that is a service contract over the term of the hosting arrangement. The guidance is effective for fiscal years beginning after December 15, 2019, and interim periods within those fiscal years. The Company does not expect the adoption of this guidance to have a material impact on its consolidated financial statements.

In August 2018, the FASB issued ASU No. 2018-13, *"Fair Value Measurement (Topic 820): Disclosure Framework — Changes to the Disclosure Requirements for Fair Value Measurement"*, an amendment to the accounting guidance on fair value measurements. The guidance modifies the disclosure requirements on fair value measurements, including the removal of disclosures of the amount of and reasons for transfers between Level 1 and Level 2 of the fair value hierarchy, the policy for timing of transfers between levels, and the valuation processes for Level 3 fair value measurements. The guidance also adds certain disclosure requirements related to Level 3 fair value measurements. The guidance is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. The Company does not expect the adoption of this guidance to have a material impact on its consolidated financial statements.

In January 2017, the FASB issued ASU No. 2017-04 "*Intangibles – Goodwill and Other (Topic 350): Simplifying the Accounting for Goodwill Impairment*," or ASU 2017-04. ASU 2017-04 allows companies to apply a one-step quantitative test and record the amount of goodwill impairment as the excess of a reporting unit's carrying amount over its fair value, not to exceed the total amount of goodwill allocated to the reporting unit. The amendments of the ASU are effective for annual or interim goodwill impairment tests in fiscal years beginning after December 15, 2019. Early adoption is permitted for interim or annual goodwill impairment tests performed on testing dates after January 1, 2017. The Company does not expect the adoption of this guidance to have a material impact on its consolidated financial statements.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"), an amendment which modifies the measurement and recognition of credit losses for most financial assets and certain other instruments. The amendment updates the guidance for measuring and recording credit losses on financial assets measured at amortized cost by replacing the "incurred loss" model with an "expected loss" model. Accordingly, these financial assets will be presented at the net amount expected to be collected. The amendment also requires that credit losses related to available-for-sale debt securities be recorded as an allowance through net income rather than reducing the carrying amount under the current, other-than-temporary-impairment model. The guidance is effective for fiscal years beginning after December 15, 2019, for public business entities that meet the definition of an SEC filer, excluding entities eligible to be Smaller Reporting Companies (SRCs) as defined by the SEC. For all other public entities, including the Company, ASU 2016-13 is effective for fiscal years beginning after December 15, 2022. The Company does not expect the adoption of this guidance to have a material impact on its consolidated financial statements.

Recently Adopted Accounting Pronouncements

On January 1, 2019, the Company adopted ASU 2016-02, *Leases (Topic 842)* along with related clarifications and improvements. This pronouncement requires lessees to recognize a liability for lease obligations with lease terms greater than twelve months, which represents the discounted obligation to make future lease payments, and a corresponding right-of-use asset on the balance sheet. The guidance also changes the definition of a lease and expands required disclosures of key information about leasing arrangements that is intended to give financial statement users the ability to assess the amount, timing, and potential uncertainty of cash flows related to leases. The Company elected the optional transition method to apply the standard as of the effective date and therefore, did not restate prior periods to apply the standard to the comparative periods presented in our consolidated financial statements.

The Company elected practical expedients as follows as of January 1, 2019:

Practical expedient package	The Company has not reassessed whether any expired or existing contracts are, or contain, leases.
	The Company has not reassessed the lease classification for any expired or existing leases.
	The Company has not reassessed initial direct costs for any expired or existing leases.
Hindsight practical expedient	The Company has not elected the hindsight practical expedient, which permits the use of hindsight when determining lease term and impairment of operating lease assets.

As a result of adopting ASC 842 as of January 1, 2019, the Company recorded an operating lease right-of-use asset of $489,000 and related operating lease liability of $491,000, respectively, related to the Company's office lease, based on the present value of the future lease payments on the date of adoption.

No other new accounting pronouncement issued or effective during the fiscal period had or is expected to have a material impact on the Company's consolidated financial statements or disclosures.

Note 3. Prepaid Expenses, Other Assets, Accrued Expenses and Other Liabilities

Prepaid expenses and other current assets consisted of the following as of December 31, 2019 and 2018 (in thousands):

	As of December 31,	
	2019	2018
Prepaid insurance	$ 734	$ 413
Prepaid clinical	102	208
Prepaid other	45	53
Insurance receivable	245	594
Other current assets	54	36
Total prepaid expenses and other current assets	$ 1,180	$ 1,304

Accrued expenses and other liabilities consisted of the following as of December 31, 2019 and 2018 (in thousands):

	As of December 31,	
	2019	2018
Accrued compensation and related expenses	$ 40	$ 742
Accrued clinical	437	735
Accrued professional services	130	194
Accrued vacation	199	160
Accrued other	7	14
Total accrued expenses and other liabilities	$ 813	$ 1,845

Note 4. Goodwill

The changes in the carrying amount of goodwill consisted of the following for the years ended December 31, 2019 and 2018 (in thousands):

	Gross Carrying Amount	Accumulated Impairment Losses	Net Carrying Amount
Balance as of December 31, 2017	$ 1,867	$ —	$ 1,867
Impairments	—	—	—
Balance as of December 31, 2018	1,867	—	1,867
Impairments		(1,867)	(1,867)
Balance as of December 31, 2019	$ 1,867	$ (1,867)	$ —

The Company performed a goodwill impairment test as of December 31, 2019 and determined that the fair value of its goodwill was below its carrying value. As a result, the Company recognized $1.9 million of goodwill impairment. No impairment was recorded for the year ended December 31, 2018.

Note 5. Commitments and Contingencies

Operating Leases

The Company leases office space under various operating leases. Total rent expense for all operating leases in the consolidated statements of operations and comprehensive loss was approximately $188,000 and $170,000 for the years ended December 31, 2019 and 2018, respectively.

In September 2015, the Company entered into a three-year operating lease for 5,197 square feet of office space in Irvine, California. The lease had an initial expiration date of August 31, 2018; however, the Company extended the term of the lease through September 30, 2021 by amending the office lease effective October 31, 2018.

The Company determines if a contract contains a lease at inception. Our material operating lease consists of a single office space. Our office lease has a remaining term of 1.75 years and does not include options to extend the lease for additional periods.

Operating lease assets and liabilities are recognized at the lease commencement date. Operating lease liabilities represent the present value of lease payments not yet paid. Operating lease assets represent our right to use an underlying asset and are based upon the operating lease liabilities as adjusted for prepayments or accrued lease payments, initial direct costs, lease incentives, and impairment of operating lease assets. To determine the present value of lease payments not yet paid, we estimate incremental secured borrowing rates corresponding to the maturities of the leases. As we have no outstanding debt nor committed credit facilities, secured or otherwise, we estimate this rate based on prevailing financial market conditions, comparable company and credit analysis, and management’s judgment.

Our leases typically contain rent escalations over the lease term. We recognize expense for these leases on a straight-line basis over the lease term. Additionally, tenant incentives used to fund leasehold improvements are recognized when earned and reduce our right-of-use asset related to the lease. These are amortized through the right-of-use asset as reductions

of expense over the lease term. Our lease agreement does not contain any material residual value guarantees or material restrictive covenants. The Company has no lease agreements with lease and non-lease components.

Related to the adoption of Topic 842, our policy elections were as follows:

Separation of lease and non-lease components	While we do not currently have any lease agreement with lease and non-lease components, we elected this expedient to account for lease and non-lease components as separate components.
Short-term policy	We have elected the short-term lease recognition exemption for all applicable classes of underlying assets. Short-term disclosures include only those leases with a term greater than one month and 12 months or less, and expense is recognized on a straight-line basis over the lease term. Leases with an initial term of 12 months or less, that do not include an option to purchase the underlying asset that we are reasonably certain to exercise, are not recorded on the consolidated balance sheet.

The components of lease expense were as follows:

	For the Year Ended December 31, 2019
Operating lease cost[(a)]	$ 196

(a) Includes variable operating lease expenses, which are immaterial.

Other information related to leases was as follows (in thousands, except lease term and discount rate):

	For the Year Ended December 31, 2019
Supplemental Cash Flows Information	
Cash paid for amounts included in the measurement of lease liability:	
Operating cash flows from operating lease	$ 180
Operating lease asset obtained in exchange for lease liability:	
Operating lease	489
Remaining lease term	
Operating lease	1.75
Discount rate	
Operating lease	3.25%

Future payments under noncancelable operating leases having initial or remaining terms of one year or more are as follows for the succeeding fiscal year and thereafter (in thousands):

As of December 31, 2019

Years ending

2020	188
2021	146
Total minimum lease payments	334
Less imputed interest	(10)
Present value of lease liabilities	324
Less current portion	(180)
	$ 144

As of December 31, 2018

Years ending

2019	180
2020	188
2021	146
Total minimum lease payments	$ 514

Grants and Licenses

Israeli Innovation Authority Grant

From 2012 through 2015, the Company received grants in the amount of approximately $537,000 from the Israeli Innovation Authority (previously the Office of Chief Scientist) of the Israeli Ministry of Economy and Industry designated for investments in research and development. The grants are linked to the U.S. dollar and bear annual interest of LIBOR. The grants are to be repaid as royalties from sales of the products developed by the Company from their investments in research and development. Because the Company has not yet earned revenues related to these investments and cannot estimate potential royalties, no liabilities related to these grants have been recorded as of each period presented. Repayment of the grant is contingent upon the successful completion of the Company's research and development programs and generating sales. The Company has no obligation to repay these grants, if the research and development program fails, is unsuccessful or aborted or if no sales are generated. The Company had not yet generated sales as of December 31, 2019; therefore, no liability was recorded for the repayment in the accompanying consolidated financial statements.

Otodyne License Agreement

In November 2015, the Company entered into an exclusive license agreement with Scientific Development and Research, Inc. and Otodyne, Inc. (collectively, the "Licensors") granting it exclusive worldwide rights to develop and commercialize OP0201, a potential first-in-class treatment option for patients at risk for or with otitis media (middle ear inflammation with or without infection), which is often caused by ETD. Under the terms of the agreement, the Company is obligated to use commercially reasonable efforts to seek approval for and commercialize at least one product for otitis media in the U.S. and key European markets (France, Germany, Italy, Spain, and the United Kingdom). The Company is responsible for prosecuting, maintaining, and enforcing all intellectual property and will be the sole owner of improvements. Under the agreement with the Licensors, the Company paid license fees totaling $750,000 and issued 9,780 common shares to the Licensors, which was expensed to research and development during the year ended December 31, 2015.

In December 2015, the Licensors completed transfer of all technology, including the active IND application to the Company. The Company is obligated to pay up to $42.1 million in development and regulatory milestones if OP0201 is approved for three indications in the United States, two in Europe, and two in Japan. The Company is also obligated to pay up to $36.0 million in sales based milestones, beginning with sales exceeding $1.0 billion in a calendar year. The Company is also obligated to pay a tiered royalty for a period up to eight years, on a country-by-country basis. The royalty ranges from a low-single to mid-single percentage of net sales. The Company made a $300,000 milestone payment in March 2019 related to the first patient enrolled in a phase 2 study, which is included in research and development expenses in 2019. There were no other milestones achieved during the years ended December 31, 2019 or 2018.

Legal Matters

The Company is involved in various lawsuits and claims arising in the ordinary course of business, including actions with respect to intellectual property, employment, and contractual matters. In connection with these matters, the Company assesses, on a regular basis, the probability and range of possible loss based on the developments in these matters. A liability is recorded in the financial statements if it is believed to be probable that a loss has been incurred and the amount of the loss can be reasonably estimated. Because litigation is inherently unpredictable and unfavorable results could occur, assessing contingencies is highly subjective and requires judgments about future events. The Company regularly reviews outstanding legal matters to determine the adequacy of the liabilities accrued and related disclosures. The amount of ultimate loss may differ from these estimates. Each matter presents its own unique circumstances, and prior litigation does not necessarily provide a reliable basis on which to predict the outcome, or range of outcomes, in any individual proceeding. Because of the uncertainties related to the occurrence, amount, and range of loss on any pending litigation or claim, the Company does not consider a liability probable and is currently unable to predict their ultimate outcome, and, with respect to any pending litigation or claim where no liability has been accrued, to make a meaningful estimate of the reasonably possible loss or range of loss that could result from an unfavorable outcome. In the event that opposing litigants in outstanding litigation proceedings or claims ultimately succeed at trial and any subsequent appeals on their claims, any potential loss or charges in excess of any established accruals, individually or in the aggregate, could have a material adverse effect on the Company's

business, financial condition, results of operations, and/or cash flows in the period in which the unfavorable outcome occurs or becomes probable, and potentially in future periods.

Legal Proceedings

On September 22, 2014, Tokai, the legal predecessor of the Company, completed the initial public offering of its common stock (the "IPO"). Subsequent to the IPO, several lawsuits were filed against Tokai, Jodie P. Morrison, Lee H. Kalowski, Seth L. Harrison, Timothy J. Barberich, David A. Kessler, Joseph A. Yanchik, III, and the underwriters of the IPO. The lawsuits allege that, in violation of the Securities Act of 1933 ("the Securities Act"), Tokai's registration statement for the IPO made false and misleading statements and omissions about Tokai's clinical trials for galeterone. Each lawsuit sought, among other things, unspecified compensatory damages, interest, costs, and attorneys' fees. Further details on each lawsuit are set forth below. The Company intends to vigorously defend against these claims. Given the uncertainty of litigation, the preliminary stage of these cases, and the legal standards that must be met for, among other things, success on the merits, the Company is unable to predict the ultimate outcome of these actions, and therefore it cannot estimate the reasonably possible loss or range of loss that may result from these actions.

- Angelos Action. On July 25, 2017, a purported stockholder of Tokai filed a lawsuit in the U.S. District Court for the District of Massachusetts, entitled *Peter B. Angelos v. Tokai Pharmaceuticals, Inc., et al.*, No. 1:17-cv-11365-MLW. On September 7, 2018, plaintiff filed an amended complaint. Defendants moved to dismiss the amended complaint on October 15, 2018. Plaintiff opposed defendants' motion on November 19, 2018, defendants filed a reply in support of their motion on December 17, 2018, and plaintiff filed a sur-reply in support of his opposition on January 8, 2019. On February 18, 2020, the court held a hearing on defendants' motion to dismiss. The court also ordered the parties to confer and notify it by March 10, 2020, if they reached an agreement to settle the case.
- Jackie888 Action. On August 19, 2016, a purported stockholder of Tokai filed a putative class action lawsuit in the Superior Court of the State of California, County of San Francisco, entitled *Jackie888, Inc. v. Tokai Pharmaceuticals, Inc., et al.*, No. CGC-16-553796. The plaintiff sought to represent a class of purchasers of Tokai common stock in or traceable to Tokai's IPO. On October 19, 2016, the defendants moved to dismiss or stay the action on grounds of forum non conveniens, and certain individual defendants moved to quash the plaintiff's summons for lack of personal jurisdiction. On February 27, 2017, the Superior Court entered an order granting defendants' motion to stay the lawsuit. On May 24, 2018, the plaintiff dismissed its complaint in the Superior Court of the State of California and refiled its complaint in the Business Litigation Session of the Superior Court Department of the Suffolk County Trial Court, Massachusetts ("Massachusetts State Court"). On June 28, 2018, plaintiff Wu moved to consolidate the Jackie888 Action with the Wu Action (discussed below). On June 29, 2018, plaintiffs Jackie888 and Wu filed a consolidated complaint. On July 6, 2018, the Jackie888 Action was consolidated with the Wu Action. Events that occurred while the actions were consolidated are described below. The Jackie888 Action and Wu Action were later de-consolidated on May 16, 2019 when the Wu Action was dismissed with prejudice. In the remaining Jackie888 action, the plaintiff filed a motion for class certification on August 22, 2019. Defendants opposed the plaintiff's motion, and the Court held a hearing on the motion for class certification on October 23, 2019. On November 25, 2019, the court denied the plaintiff's motion for class certification. On December 23, 2019, the court granted the parties' stipulation to dismiss the case with prejudice.

- Wu Action. On December 5, 2016, a putative securities class action was filed in the Massachusetts State Court, entitled *Wu v. Tokai Pharmaceuticals, Inc., et al.,* 16-3725 BLS ("Wu Action"). The plaintiff seeks to represent a class of purchasers of Tokai common stock in or traceable to Tokai's IPO. On December 19, 2016, defendants removed the Wu Action to the U.S. District Court for the District of Massachusetts, where it was captioned *Wu v. Tokai Pharmaceuticals, Inc., et al.,* 16-cv-12550. On January 6, 2017, plaintiff filed a motion to remand the Wu Action to Massachusetts State Court. On September 28, 2017, the court stayed the case pending a decision by the United States Supreme Court in *Cyan, Inc. v. Beaver County Employees Retirement Fund*, S. Ct. Case No. 15-1439. On March 20, 2018, the United States Supreme Court ruled in *Cyan* that state courts have subject matter jurisdiction over covered class actions alleging only Securities Act claims and that such actions are not removable to federal court. On March 22, 2018, plaintiff moved for leave to submit the *Cyan* decision in support of plaintiff's remand motion. On March 27, 2018 the Wu Action was remanded to the Massachusetts State Court. On May 3, 2018, plaintiff filed an amended class action complaint. Following the refiling of the Jackie888 Action in Massachusetts State Court (discussed above), on June 28, 2018, plaintiff Wu moved to consolidate the Jackie888 Action with the Wu Action. On June 29, 2018, plaintiffs Jackie888 and Wu filed a consolidated complaint. On July 6, 2018, the Jackie888 Action was consolidated with the Wu Action. Defendants moved to dismiss the consolidated complaint on August 15, 2018, plaintiffs filed their opposition thereto on September 28, 2018, and defendants filed their reply in support of their motion on October 19, 2018. In addition, Defendants moved to strike the class allegations in the consolidated complaint on August 15, 2018, plaintiffs filed their opposition thereto on September 11, 2018, and defendants filed their reply in support of their motion on September 21, 2018. The court held a hearing on November 15, 2018 on defendants' motion to strike. On December 20, 2018, the court denied defendants' motion to strike. The court held a hearing on December 20, 2018 on defendants' motion to dismiss. On January 8, 2019, the court denied defendants' motion to dismiss. On February 6, 2019, the court entered a scheduling order, pursuant to which discovery on merits issues was stayed pending the court's resolution of class certification. On April 18, 2019, the court held a hearing as to plaintiff Wu's failure to respond to defendant's discovery requests. The court issued an order requiring plaintiff Wu to serve written responses to the pending discovery requests by May 10, 2019. Plaintiff Wu failed to serve written responses by the deadline and her claims were subsequently dismissed with prejudice by the court on May 16, 2019.

Indemnification

In the normal course of business, the Company enters into contracts and agreements that contain a variety of representations and warranties and provide for general indemnification. The Company's exposure under these agreements is unknown because it involves future claims that may be made against the Company but have not yet been made. To date, the Company has not paid any claims or been required to defend any action related to its indemnification obligations. However, the Company may record charges in the future because of these indemnification obligations. No amounts associated with such indemnifications have been recorded to date.

Contingencies

From time to time, the Company may have certain contingent liabilities that arise in the ordinary course of business activities. The Company accrues a liability for such matters when it is probable that future expenditures will be made and such expenditures can be reasonably estimated. There have been no contingent liabilities requiring accrual at December 31, 2019 and 2018.

Note 6. Stock-Based Compensation

The Company has two stock compensation plans, the 2014 Stock Incentive Plan (the "2014 Plan") and the 2007 Stock Incentive Plan (the "2007 Plan"). The 2014 Plan permits the Company to make grants of incentive stock options, non-statutory stock options, restricted stock, restricted stock units, stock appreciation rights and other stock-based awards to the Company's employees, officers, directors, consultants and advisors; however, incentive stock options may only be granted to the Company's employees. The number of shares initially reserved for issuance under the 2014 Plan was 1,700,000 shares of common stock and may be increased by the number of shares under the 2007 Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company. The number of shares of common stock that may be issued under the plan is also subject to an annual increase on the first day of each fiscal year equal to the lesser of (i) 1,800,000 shares of the Company's common stock, (ii) 4% of the number of shares of the Company's common stock outstanding on the first day of the applicable fiscal year or (iii) an amount determined by the Company's board of directors. Options remain outstanding under both the 2007 and the 2014 Plan. The number of shares subject to and the exercise prices applicable to

these outstanding options were adjusted in connection with the one for nine reverse stock-split. As of December 31, 2019, there were 84,612 options outstanding under the 2007 plan. Options granted under the 2007 and 2014 Plans generally expire ten years from the date of grant. The Company intends for the 2014 Plan to be its primary stock compensation plan in the future.

Effective as of August 1, 2018, the Board of Directors amended the Company's 2014 Stock Incentive Plan (the "2014 Plan") and the Company's 2014 Employee Stock Purchase Plan (the "ESPP" and, together with the 2014 Plan, the "Plans") to reduce the share reserves under the Plans. These reductions were made to equitably adjust the share reserves in accordance with the terms of the Plans. As a result of these equitable adjustments: (1) the number of shares of common stock authorized for issuance under the 2014 Plan (excluding shares underlying outstanding awards as of August 1, 2018) was reduced to 766,500 shares and the maximum number of shares that can be added to the 2014 Plan under evergreen provision set forth in Section 4(a)(1)(C) of the 2014 Plan was reduced to 550,000 shares annually; and (2) the number of shares of common stock authorized for future issuance under the ESPP was reduced to 209,500 shares (excluding shares previously issued under the ESPP prior to August 1, 2018) and the maximum number of shares that can be added to the ESPP under the evergreen provision set forth in the ESPP was reduced to 135,000 shares annually. The 2014 Plan and ESPP were amended and restated as of August 1, 2018 to reflect these equitable adjustments.

Stock Option and PRSU Activity

As of December 31, 2019, a total of 337,955 stock awards were available for grant under the 2014 Plan.

The following table shows the stock option and PRSU activity, as follows:

	Shares Issuable Under Options and PRSUs	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
			(In years)	(In thousands)
Outstanding as of January 1, 2018	782,340	$ 14.28	8.8	$ 8.5
Granted	267,950	5.02		
Exercised	(15,120)	4.74		
Forfeited / Canceled	(60,353)	7.31		
Outstanding as of December 31, 2018	974,817	12.31	8.2	—
Granted	815,400	1.75		
PRSUs vested	(78,450)	4.83		
Forfeited / Canceled	(11,500)	4.41		
Outstanding as of December 31, 2019	1,700,267	$ 7.64	8.2	$ —
Stock awards vested and expected to vest as of December 31, 2019	1,645,267	$ 7.64	8.2	$ —
Options exercisable as of December 31, 2019	882,576	$ 12.49	7.3	$ —

As of December 31, 2019, the range of exercise prices was between $0.67 and $119.25 for options outstanding.

Intrinsic value is calculated as the difference between the exercise price of the underlying options and the fair value of the common stock for the options that had exercise prices that were lower than the fair value per share of the common stock on the date of exercise. There was no aggregate intrinsic value of options exercised during the years ended December 31, 2019 and 2018.

As of December 31, 2019, total unrecognized stock-based compensation expense related to non-vested equity awards was $1.3 million, which is expected to be recognized over an estimated weighted-average period of 2.2 years.

Stock-based Compensation Expense

Total compensation expense related to all of the Company's stock-based awards for the years ended December 31, 2019 and 2018 was comprised of the following (in thousands):

	Year Ended December 31,	
	2019	2018
Stock-based compensation classified as:		
Research and development expense	$ 343	$ 249
General and administrative expense	965	1,294
Total stock-based compensation expense	$ 1,308	$ 1,543

Stock-based compensation expense for the year ended December 31, 2019 included no stock-based compensation expense related to a performance-based option granted during 2019.

During the year ended December 31, 2019, PRSUs awarded to employees totaling 78,450 shares vested and resulted in the recognition of $379,000 in stock-based compensation expense.

Valuation Assumptions

The following table presents the assumptions used in the Black-Scholes option pricing model to determine the fair value of stock options granted in the periods presented, as follows:

	Year Ended December 31,	
	2019	2018
Expected stock price volatility	74% - 87%	63% - 86%
Risk-free interest rate	1% - 3%	2% - 3%
Expected life of option (in years)	6	5 - 7
Estimated dividend yield	0%	0%

Note 7. Income Taxes

Loss before income taxes are as follows (in thousands):

	Year Ended December 31,	
	2019	2018
Losses before income taxes:		
U.S.	$ (16,174)	$ (14,177)
Non-U.S.	163	112
Total	$ (16,011)	$ (14,065)

The provision (benefit) for income taxes are as follows (in thousands):

	Year Ended December 31,	
	2019	2018
Current:	$ —	$ —
Federal	—	—
State	—	—
Foreign	—	—
	—	—
Deferred		
Federal	—	—
State	—	—
Foreign	—	—
	—	—
Provision (benefit) for income taxes	$ —	$ —

The Company is subject to income taxes under U.S. tax laws. The Company was subject to an Israeli corporate tax rate of 23% in 2018. The Company is subject to an Israeli corporate tax rate of 23% in 2019 and thereafter. The Company was subject to a blended U.S. tax rate (federal as well as state corporate tax) of 21% in 2018 and 2019.

The SEC staff issued Staff Accounting Bulletin No. 118 ("SAB 118"), which provides guidance on accounting for the tax effects of H.R. 1/Public Law No. 115-97, known as the Tax Cuts and Jobs Act (the "Tax Act"). SAB 118 provides a measurement period that should not extend beyond one year from the Tax Act enactment date for companies to complete the accounting under ASC 740. In accordance with SAB 118, a company must reflect the income tax effects of those aspects of the Tax Act for which the accounting under ASC 740 is complete. To the extent that a company's accounting for certain income tax effects of the Tax Act is incomplete but it is able to determine a reasonable estimate, it must record a provisional estimate in the financial statements. If a company cannot determine a provisional estimate to be included in the financial statements, it should continue to apply ASC 740 on the basis of the provisions of the tax laws that were in effect immediately before the enactment of the Tax Act. As of December 22, 2018, the Company's accounting for the remeasurement of its deferred tax assets was complete and there were no changes to the amount previously recorded.

Significant judgment is required in determining the Company's provision for income taxes, deferred tax assets and liabilities and the valuation allowance recorded against net deferred tax assets. Deferred tax assets and liabilities are determined using the enacted tax rates in effect for the years in which those tax assets are expected to be realized. A valuation allowance is established when it is more likely than not the future realization of all or some of the deferred tax assets will not be achieved. The evaluation of the need for a valuation allowance is performed on a jurisdiction-by-jurisdiction basis, and includes a review of all available positive and negative evidence. Factors reviewed include projections of pre-tax book income for the foreseeable future, determination of cumulative pre-tax book income after permanent differences, earnings history, and reliability of forecasting.

Based on its review, the Company concluded that it was more likely than not that they would not realize the benefit of its deferred tax assets in the future. This conclusion was based on historical and projected operating performance, as well as the Company's expectation that its operations will not generate sufficient taxable income in future periods to realize the tax benefits associated with the deferred tax assets within the statutory carryover periods. Therefore, the Company maintained a full valuation allowance on its deferred tax assets as of December 31, 2019 and 2018.

The Company will continue to assess the need for a valuation allowance on its deferred tax assets by evaluating both positive and negative evidence that may exist. Any adjustment to the net deferred tax asset valuation allowance would be recorded in the statement of operations for the period that the adjustment is determined to be required.

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,	
	2019	2018
Statutory Federal income tax rate	$ (3,362)	$ (2,953)
State income taxes, net of Federal tax benefits	—	—
Foreign losses	—	—
Tax credits	(207)	(204)
Change in statutory rates	—	—
Stock-based compensation	141	72
Goodwill impairment	392	
Permanent items	4	3
Other	38	90
Change in valuation allowance	2,994	2,992
Total provision for income taxes	$ —	$ —

Significant components of the Company's deferred tax assets and liabilities as of December 31, 2019 and 2018 consisted of the following (in thousands):

	Year Ended December 31,	
	2019	2018
Net operating loss carryforwards	$ 9,947	$ 7,126
Research and development tax credits	506	299
Accruals and reserves	43	159
Stock compensation	391	301
Depreciation and amortization	116	126
Lease liability	68	—
Total deferred tax assets	11,071	8,011
Right-of-use asset	(66)	—
Total deferred tax liabilities	(66)	—
Less: valuation allowance	(11,005)	(8,011)
Net deferred tax assets	$ —	$ —

The following table reconciles the beginning and ending amounts of unrecognized tax benefits for the years presented (in thousands):

	Year Ended December 31,	
	2019	2018
Gross unrecognized tax benefits at the beginning of the year	$ 328	$ 181
Additions from tax positions taken in the current year	214	158
Additions from tax positions taken in prior years	6	—
Reductions from tax positions taken in prior years	—	(11)
Tax settlements	—	—
Gross unrecognized tax benefits at the end of the year	$ 548	$ 328

The deferred income tax assets have been fully offset by a valuation allowance, as realization is dependent on future earnings, if any, the timing and amount of which are uncertain. The net valuation allowance increased by $3.0 million.

The Company's accounting for deferred taxes involves the evaluation of a number of factors concerning the realizability of its net deferred tax assets. The Company primarily considered such factors as its history of operating losses, the nature of the Company's deferred tax assets, and the timing, likelihood, and amount, if any, of future taxable income during the periods in which those temporary differences and carryforwards become deductible. At present, the Company does not believe that it is more likely than not that the deferred tax assets will be realized; accordingly, a full valuation allowance has been established and no deferred tax asset is shown in the accompanying balance sheets.

As of December 31, 2019 and 2018, the Company had federal net operating loss carryforwards of approximately $38.6 million and $25.0 million, respectively, available to reduce future taxable income. As of December 31, 2019 and December 31, 2018, the Company also has state net operating loss carryforwards of $0.9 million. Both the federal and California net operating loss carryforwards incurred before 2018 begin expiring in 2034 if not utilized. The December 31, 2019 and 2018 federal net operating losses of $13.6 million and $12.5 million, respectively, do not expire. As of December 31, 2019 and 2018, the Company had Israeli net operating losses of $8.0 million and $8.2 million, respectively, which carryforward indefinitely.

As of December 31, 2019 and 2018, the Company had federal research and development tax credit carryforwards of approximately $764,000 and $420,000, respectively. If not utilized, the carryforwards will begin expiring in 2025. As of December 31, 2019 and 2018, the Company has state research and development credit carryforwards or approximately $264,000 and $161,000, respectively, which do not expire.

Pursuant to Internal Revenue Code ("IRC) Sections 382 and 383, annual use of the Company's net operating loss and research and development credit carryforwards may be limited in the event a cumulative change in ownership of more than 50% occurs within a three-year period. The Company has not completed an IRC Section 382/383 analysis regarding the limitation of net operating loss and research and development credit carryforwards. Due to the existence of the valuation allowance, future changes in the Company's unrecognized tax benefits will not impact the Company's effective tax rate.

The Company's ability to use its remaining net operating loss and tax credit carryforwards may be further limited if the Company experiences a Section 382 ownership change in connection with future changes in the Company's stock ownership.

In the United States, the Company files income tax returns in the U.S. Federal jurisdiction and California. The Company's tax years for 2016 and forward are subject to examination by the Federal and California tax authorities due to the carryforward of unutilized net operating losses and research and development credits.

The Company's policy is to recognize interest expense and penalties related to income tax matters as a component of income tax expense. There was no accrued interest and penalties associated with uncertain tax positions as of December 31, 2019 and 2018. The Company has not recorded any interest or penalties in 2019 or 2018.

Note 8. Stockholders' Equity

Equity Distribution Agreement

On July 23, 2018, the Company filed a prospectus and prospectus supplement (the "2018 Prospectus") under which the Company may offer and sell, from time to time, pursuant to an equity distribution agreement with Piper Jaffray & Co., up to $9.8 million in shares of its common stock. As of December 31, 2019, 25,218 shares have been sold under the 2018 Prospectus for gross proceeds of approximately $110,000. As of December 31, 2019, $8.7 million of the $9.8 million shares of common stock remains available to be offered and sold under the 2018 Prospectus.

2019 Equity Offering

On April 30, 2019, the Company agreed to sell in a registered direct offering, an aggregate 3,449,112 shares of its common stock to certain investors for gross proceeds of approximately $10.7 million under its effective shelf registration statement on Form S-3 (File No. 333-226286). In a concurrent private placement, the Company also agreed to issue to such investors Series A warrants to purchase up to 3,449,112 shares of its common stock at an exercise price of $4.00 with a term of eighteen months and Series B warrants to purchase up 3,449,112 shares of its common stock at an exercise price of $4.00 with a term of five years. The Series B warrants become exercisable only upon the exercise of the Series A warrants. In addition, the Company agreed to issue to H.C. Wainwright & Co., LLC, the placement agent for the transaction, warrants to purchase up to 172,456 shares of common stock. The placement agent warrants have substantially the same terms as the Series A Warrants, except that the placement agent warrants will have an exercise price equal to $3.86875 and will expire on April 30, 2024. We refer to the registered direct offering and the concurrent private placement collectively as the "2019 Equity Offering".

All the warrants issued in connection with the 2019 Equity Offering contained put options that allow the holders of the warrants the right to receive, for each warrant share that would have been issuable upon an exercise immediately prior to the occurrence of an effective change in control event defined as a fundamental transaction, the number of shares of common stock of the successor or acquiring corporation or of the Company, if it is the surviving corporation, and any additional

consideration receivable as a result of such fundamental transaction by a holder of the number of shares of common stock for which this warrant is exercisable immediately prior to such fundamental transaction. The Company evaluated the embedded put option contained in the warrants under the guidance of Accounting Standards Codification ("ASC") 815, *Derivatives and Hedging*, and concluded that the requirements for contingent exercise provisions as well as the settlement provision for scope exception in ASC 815-10-15-74 has been met. Accordingly, the put options contained in the warrants were not bi-furcated and accounted for as freestanding derivative instruments.

Warrants

As of December 31, 2019, a total of 7,070,680 warrants were available for exercise.

The following table shows the warrant activity (in thousands):

	Rollforward of Warrant Activity			
	Registered direct warrants, series A	**Registered direct warrants, series B**	**Registered direct warrants, placement agent**	**Total**
Balance as of January 1, 2019	—	—	—	—
Warrants issued	3,449,112	3,449,112	172,456	7,070,680
Warrants exercised	—	—	—	—
Warrants expired	—	—	—	—
Balance as of December 31, 2019	3,449,112	3,449,112	172,456	7,070,680

Note 9. Subsequent Events

Warrant Exercise Transaction

On January 10, 2020 and January 15, 2020, the Company entered into warrant exercise agreements (the "Exercise Agreements") with the holders (the "Holders") of its Series A Warrants and Series B Warrants to purchase shares of the Company's common stock (collectively, the "Warrants"), previously issued in a private placement by the Company in May 2019, pursuant to which the Holders agreed to exercise in cash their Warrants to purchase an aggregate of 6,898,224 shares of the Company's common stock at a reduced exercise price of $0.715 per share, plus an additional $0.125 per share for the issuance of the private placement warrants for gross proceeds (before placement agent fees and expenses) to the Company of approximately $5.8 million (the "Exercise Transaction").

The Company intends to use the net proceeds from the Exercise Transaction to fund the ongoing phase 2a clinical trial in acute otitis media, as well as for working capital and other general corporate purposes.

Under the Exercise Agreements, the Company also agreed to issue to the Holders new warrants to purchase up to 6,898,224 shares of the Company's common stock at an exercise price of $0.72 per share, with an exercise period of five and a half years (the "Private Placement Warrants"). The Private Placement Warrants transaction subsequently closed and the Private Placement Warrants were issued on January 14, 2020 with respect to the Warrants exercised on January 10, 2020 and on or about January 17, 2020, with respect to the Warrants exercised on January 15, 2020.

The shares of common stock underlying the Warrants are registered for offer and sale under the Securities Act of 1933, as amended (the "Securities Act"), pursuant to the Company's effective registration statement on Form S-1 (File No. 333-232011).

Common Stock Exchange Agreement

On February 13, 2020, the Company entered into an exchange agreement (the "Exchange Agreement") with Biotechnology Value Fund, L.P., Biotechnology Value Fund II, L.P. and Biotechnology Value Trading Fund OS, L.P. (the "Exchanging Stockholders"), pursuant to which the Exchanging Stockholders exchanged (the "Exchange") 3,796,000 shares of the Company's common stock, par value $0.001 per share (the "Common Stock"), for 3,796 shares of newly designated Series X Convertible Preferred Stock (the "Series X Preferred Stock"). The Company agreed to reimburse the Exchanging Stockholders for their expenses in connection with the Exchange up to a total of $25,000.

On February 13, 2020, in connection with the Exchange, the Company filed a Certificate of Designation (the "CoD") setting forth the preferences, rights and limitations of the Series X Preferred Stock with the Secretary of State of the State of Delaware. Each share of Series X Preferred Stock will be convertible into 1,000 shares of Common Stock at the option of the holder at any time; subject to certain limitations, including, that the holder will be prohibited from converting Series X Preferred Stock into Common Stock if, as a result of such conversion, the holder, together with its affiliates, would beneficially own a number of shares of Common Stock above a conversion blocker, which is initially set at 9.99% of the total Common Stock then issued and outstanding immediately following the conversion of such shares of Series X Preferred Stock. In the event of the Company's liquidation, dissolution or winding up, holders of Series X Preferred Stock will participate pari passu with any distribution of proceeds to holders of Common Stock. Holders of Series X Preferred Stock are entitled to receive dividends on shares of Series X Preferred Stock equal (on an as-if-converted-to-Common Stock basis) to and in the same form as dividends actually paid on the Common Stock or other junior securities of the Company. Shares of Series X Preferred Stock will generally have no voting rights, except as required by law and except that the consent of a majority of the holders of the outstanding Series X Preferred Stock will be required to amend the terms of the Series X Preferred Stock.

The Series X Preferred Stock was issued without registration under the Securities Act of 1933, as amended (the "Securities Act"), in reliance on the exemption from registration contained in Section 3(a)(9) of the Securities Act.

The Exchange was completed on February 19, 2020. Following the Exchange, the Company had 16,069,562 shares of Common Stock outstanding and 3,796 shares of Series X Preferred Stock outstanding, which are convertible into 3,796,000 shares of Common Stock.