OTONOMY, INC.
Form 10-K
March 08, 2018

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, 2017

OR

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

Commission File Number 001-36591

Otonomy, Inc.

(Exact name of registrant as specified in its Charter)

Delaware	26-2590070
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

4796 Executive Drive

San Diego, California 92121

(Address of principal executive offices and Zip Code)

(619) 323-2200

(Registrant's telephone number, including area code)

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

Title of each class	Name of each exchange on which registered
Common stock, par value $0.001 per share	The NASDAQ Stock Market LLC
	(The NASDAQ Global Select Market)

Securities registered pursuant to Section 12(g) of the Act: None

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

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

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). YES NO

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

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

Large accelerated filer		Accelerated filer
Non-accelerated filer	(Do not check if a smaller reporting company)	Smaller reporting company
Emerging growth company		

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

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

The aggregate market value of the common stock held by non-affiliates of the registrant as of June 30, 2017 (the last business day of the registrants most recently completed second fiscal quarter) was approximately $357.7 million based on the closing price of the registrant's common stock, as reported by the NASDAQ Global Select Market on June 30, 2017 of $18.85 per share. Shares of the registrant's common stock held by each executive officer, director and holder of 10% or more of the outstanding common stock have been excluded in that such persons may be deemed to be affiliates. This calculation does not reflect a determination that certain persons are affiliates of the registrant for any other purpose.

As of March 2, 2018, the number of outstanding shares of the registrant's common stock, par value $0.001 per share, was 30,577,526.

DOCUMENTS INCORPORATED BY REFERENCE

As noted herein, the information called for by Part III is incorporated by reference to specified portions of the registrant's definitive proxy statement to be filed in conjunction with the registrant's 2018 Annual Meeting of Stockholders, which is expected to be filed not later than 120 days after the registrant's fiscal year ended December 31, 2017.

OTONOMY, INC.

ANNUAL REPORT ON FORM 10-K

FOR THE YEAR ENDED December 31, 2017

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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, as Section 21E of the Securities Exchange Act of 1934, as amended, which statements involve substantial risks and uncertainties. Forward-looking statements generally relate to future events or our future financial or operating performance. In some cases, you can identify forward-looking statements because they contain words such as “anticipate,” “believe,” “could,” “estimate,” “expects,” “intend,” “may,” “plan,” “potential,” “predi “should,” “will,” “would” the negative of those terms, and similar expressions that convey uncertainty of future events or outcomes. Forward-looking statements contained in this Annual Report on Form 10-K include, but are not limited to, statements about:

- our expectations regarding commercial partnering options for OTIRIO, including divestiture;
- our expectations regarding our clinical development of OTIVIDEX, including but not limited to the timing of initiation of a pivotal clinical trial in mid-2018;
- our expectations regarding the clinical development of OTO-313, including but not limited to our plans to initiate a Phase 1/2 clinical trial in tinnitus patients in the first half of 2019;
- our expectations regarding the clinical development of OTO-413, including but not limited to our plans to initiate a Phase 1/2 clinical trial in hearing loss patients in the first half of 2019;
- the timing or likelihood of regulatory filings and approvals;
- our expectations regarding the future development of other product candidates, including but not limited to our plans to select a candidate for clinical development for both the OTO-5XX and OTO-6XX programs in the second half of 2018;
- the potential for commercialization of our product candidates, if approved;
- our expectations and statements regarding the pricing, market size, opportunity and growth potential for OTIVIDEX, OTO-313, OTO-413 and our other product candidates, if approved for commercial use;
- our expectations and statements regarding the adoption and use of OTIPRIO and OTIVIDEX, OTO-313 and OTO-413, if approved, by ear, nose and throat physicians (ENTs);
- our expectations regarding potential coverage and reimbursement relating to OTIPRIO, and OTIVIDEX, OTO-313 and OTO-413, if approved, or any other approved product candidates;
- our plans regarding the use of contract manufacturers for the production of our product candidates for clinical trials and, if approved, commercial use;
- our plans and ability to effectively establish and manage our own sales and marketing capabilities, or seek and establish collaborative partners, to commercialize our products;
- our ability to advance product candidates into, and successfully complete, clinical trials;
- the implementation of our business model, strategic plans for our business, products and technology;
- the initiation, timing, progress and results of future nonclinical studies and clinical trials;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our products and technology;
- estimates of our expenses, future revenue, capital requirements and our needs for additional financing;
- our financial performance;
- accounting principles, policies and estimates;
- developments and projections relating to our competitors and our industry; and
- our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including but not limited to: our limited operating history and our expectation that it we incur significant losses for the foreseeable future; our ability to obtain additional financing; our dependence on the regulatory success and advancement of our product candidates; the uncertainties inherent in the clinical drug development process, including, without limitation, our ability to adequately demonstrate the safety and efficacy of our product candidates, the nonclinical and clinical results for our product candidates, which may not support further development, and challenges related to patient enrollment in clinical trials; our ability to obtain regulatory approval for our product candidates; side effects or adverse events associated with our product candidates; our ability to successfully commercialize our product candidates, if approved; competition in the biopharmaceutical industry; our dependence on third parties to conduct nonclinical studies and clinical trials; our dependence on third parties for the manufacture of our product candidates; our dependence on a small number of suppliers for raw materials; our ability to protect our intellectual property related to our product candidates in the United States and throughout the world; expectations regarding potential market size, opportunity and growth; our ability to manage operating expenses; implementation of our business model and strategic plans for our business, products and technology; and other risks. Information regarding the foregoing and additional risks are described in the section entitled “Risk Factors” and elsewhere in this Annual Report on Form 10-K. Moreover, we operate in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this Annual Report on Form 10-K may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. Moreover, neither we nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this Annual Report on Form 10-K to conform these statements to actual results or to changes in our expectations, except as required by law.

You should read this Annual Report on Form 10-K and the documents that we reference in this Annual Report on Form 10-K and have filed with the SEC as exhibits to this Annual Report on Form 10-K with the understanding that our actual future results, levels of activity, performance, and events and circumstances may be materially different from what we expect.

PART I

Item 1. BUSINESS

Overview

Otonomy is a biopharmaceutical company dedicated to the development of innovative therapeutics for otology. We pioneered the application of drug delivery technology to the ear in order to develop products that achieve sustained drug exposure from a single local administration. This approach is covered by a broad patent estate and is being utilized to develop a pipeline of products addressing important unmet medical needs including Ménière's disease, hearing loss and tinnitus.

OTIVIDEX™ is a steroid in development for the treatment of Ménière's disease. Two Phase 3 trials in Ménière's disease patients were completed in the second half of 2017. The AVERTS-2 trial, conducted in Europe, achieved its primary endpoint (p value = 0.029), while the AVERTS-1 trial, conducted in the United States, did not (p value = 0.62). Based on a recent Type C meeting with the United States Food and Drug Administration (FDA), we believe that one additional successful pivotal trial is sufficient to support the U.S. registration of OTIVIDEX in Ménière's disease. We expect to initiate this trial in mid-2018.

Gacyclidine is a potent and selective N-Methyl-D-Aspartate (NMDA) receptor antagonist in development for the treatment of tinnitus. A Phase 1 clinical safety trial has been successfully completed using OTO-311, a poloxamer-based formulation of gacyclidine, with no safety concerns observed. We have shifted development to OTO-313, an alternative formulation of gacyclidine that has improved properties compared to OTO-311, and expect to initiate a Phase 1/2 clinical trial for OTO-313 in tinnitus patients in the first half of 2019.

We are advancing three distinct hearing loss programs that address different pathologies and broad patient populations. OTO-413 is a sustained exposure formulation of brain-derived neurotrophic factor (BDNF) in development for the repair of cochlear synaptopathy and the treatment of speech-in-noise hearing difficulties. We have initiated nonclinical studies and manufacturing for OTO-413 to support an Investigational New Drug (IND) Application, with a Phase 1/2 clinical trial expected to begin in hearing loss patients in the first half of 2019. OTO-5XX is an otoprotectant in development for the prevention of cisplatin-induced hearing loss (CIHL). OTO-6XX induces hair cell regeneration in a nonclinical proof-of-concept model and is being developed for the treatment of severe hearing loss. We expect to select a candidate for clinical development for both the OTO-5XX and OTO-6XX programs in the second half of 2018.

In addition, we developed, received FDA approval and commercially launched OTIPRIO® (ciprofloxacin otic suspension) for use during tympanostomy tube placement (TTP) surgery in pediatric patients. OTIPRIO was also recently approved by the FDA for the treatment of acute otitis externa (AOE). In November 2017, we announced the discontinuation of promotional support for OTIPRIO in order to significantly reduce operating expenses related to the product. OTIPRIO continues to be available for purchase by customers while we evaluate commercial partnering options for the product, including divestiture.

Our Product Pipeline

The following table summarizes the status of our product candidates currently in development and the indications for our approved product, and is followed by a brief description of each program:

Program (Compound)	Target Population	Next Milestone
OTIVIDEX (dexamethasone)	Ménière's Disease	Initiate Phase 3 trial in mid-18
OTO-313 (gacyclidine)	Tinnitus	Initiate Phase 1/2 in 1H19
OTO-413 (BDNF)	Synaptopathy Hearing Loss	Initiate Phase 1/2 in 1H19
OTO-5XX (otoprotectant)	Cisplatin-Induced Hearing Loss	Candidate Selection in 2H18
OTO-6XX (hair cell regeneration)	Severe Hearing Loss	Candidate Selection in 2H18
OTIPRIO (ciprofloxacin)	TTP Surgery Acute Otitis Externa	Commercial Partnership or Divestiture

OTIVIDEX: Sustained-Exposure Steroid for Ménière's Disease

OTIVIDEX is a sustained-exposure formulation of the steroid dexamethasone in development for the treatment of Ménière's disease. Ménière's disease is a chronic condition characterized by acute vertigo attacks, tinnitus, fluctuating hearing loss and a feeling of aural fullness. The underlying cause of Ménière's disease is not well understood and there is no known cure. There are more than 600,000 patients diagnosed with Ménière's disease in the United States and there are currently no FDA-approved drug treatments. Typical first line treatment in the United States is observance of a low-salt diet and off-label use of diuretics. Oral and intratympanic (IT) steroids are used in a subset of Ménière's patients who have persistent or severe symptoms. Patients who are unresponsive to steroid treatment may resort to surgical or chemical ablation, which can cause irreversible hearing loss.

In November 2017, we announced positive results from the AVERTS-2 Phase 3 clinical trial for OTIVIDEX conducted in Europe. The clinical trial achieved its primary endpoint of count of definitive vertigo days (DVD) by Poisson Regression analysis in Month 3 for OTIVIDEX vs. placebo (p value = 0.029) based on analysis of all 174 Ménière's disease patients enrolled in the trial. The OTIVIDEX group demonstrated a 6.2-day reduction in the mean reported number of DVD from baseline to Month 3 with a 2.5 day mean difference between OTIVIDEX and placebo in Month 3. For subjects who completed daily diaries through Month 3 (n=105), there was a 68% reduction in vertigo frequency from baseline to Month 3 in the OTIVIDEX group vs. 40% for placebo. In January 2018, we reported that a number of additional efficacy endpoints were also statistically significant for the 111 patients who were enrolled in the AVERTS-2 trial through Month 3 at the time of study termination, including count of DVD by Poisson Regression analysis (p value = 0.014).

In August 2017, we announced negative results from the AVERTS-1 Phase 3 clinical trial conducted in the United States that enrolled a total of 165 patients with Ménière's disease. The clinical trial missed its primary endpoint, count of DVD by Poisson Regression analysis in Month 3 (p value = 0.62), and also failed to achieve statistical significance (p value < 0.05) for any of the key secondary vertigo endpoints at Month 3. Patients in both the OTIVIDEX and placebo groups showed similar reductions in the number and severity of vertigo episodes during the three-month observation period. OTIVIDEX patients reported a 58% reduction from baseline in vertigo frequency in Month 3 vs. 55% for placebo patients.

The clinically significant treatment benefit demonstrated by OTIVIDEX versus placebo in AVERTS-2 was consistent with our expectations from the Phase 2b trial. We believe that the AVERTS-1 trial failed due to a significantly higher placebo response and was not attributable to a difference in patient demographics or baseline characteristics compared to AVERTS-2. A review of the AVERTS trials including consultation with outside experts suggests that the higher placebo response was primarily due to increased patient expectation bias in the U.S. trial. We have recently completed a Type C meeting with the FDA that included a review of the AVERTS and other clinical trial results. Based on FDA feedback, we believe that one additional successful pivotal trial is sufficient to support the U.S. registration of OTIVIDEX in Ménière's disease, and we expect to initiate this trial in mid-2018.

OTO-313: Sustained-Exposure NMDA Receptor Antagonist for Tinnitus

OTO-313 is a sustained-exposure formulation of the NMDA receptor antagonist gacyclidine in development for the treatment of tinnitus. Tinnitus is often described as a ringing in the ear but can also sound like roaring, clicking, hissing or buzzing. People with severe tinnitus may have trouble hearing, working and sleeping. At this time, there is no cure for tinnitus and there are no FDA-approved drugs for the treatment of this debilitating condition.

Historic and emerging clinical data provide support for the use of NMDA receptor antagonists, including gacyclidine, for the treatment of tinnitus. Mechanistically, agents from this therapeutic class may act to reduce dysfunctional activity resulting from injury to the hearing organ, or cochlea, and be perceived by the patient as tinnitus. Several clinical trials have demonstrated reductions in the severity of tinnitus and improvement in the functional status of patients following treatment with an NMDA receptor antagonist. We expect that the results of these trials will be instructive in the design and implementation of our OTO-313 clinical development program.

The goal of our OTO-313 program is to develop a sustained-exposure formulation of gacyclidine that will provide a course of treatment from a single IT injection. A Phase 1 clinical safety trial in normal healthy volunteers has been successfully completed using OTO-311, a poloxamer-based formulation of gacyclidine, with no safety concerns observed. We have shifted development to OTO-313, an alternative formulation of gacyclidine that has improved properties compared to OTO-311, and expect to initiate a Phase 1/2 clinical trial for OTO-313 in tinnitus patients in the first half of 2019.

Development Programs for the Treatment of Sensorineural Hearing Loss

Hearing loss is a large and growing unmet need with estimates by the World Health Organization that more than 360 million people worldwide have disabling levels of loss. This leads to social isolation, lower quality of life and higher rates of dementia and depression. Common causes include aging, noise, exposure to ototoxic drugs and genetics, with increased noise exposure from use of recreational music devices accelerating the onset of hearing loss. The pathologies of hearing loss typically involve damage to hair cells and/or spiral ganglion neurons in the inner ear. As briefly described below, we are advancing three distinct hearing loss programs targeting different pathologies: repair of cochlear synaptopathy for treatment of speech-in-noise difficulties (OTO-413), protection of hair cells from ototoxic drugs including cisplatin chemotherapy (OTO-5XX), and hair cell regeneration for treatment of severe hearing loss (OTO-6XX).

OTO-413: Neurotrophic Growth Factor for Speech-in-Noise Difficulties

Cochlear synaptopathy is a hearing pathology caused by damage to ribbon synapses that has become an active focus of otology research in the last decade. Ribbon synapses are critical to hearing because they connect sound transducers in the cochlea called hair cells to auditory nerve fibers, which carry the electrical sound impulse to the brain for interpretation. Damage to ribbon synapses can be caused by exposure to loud noise and/or aging, and results in hearing problems in the presence of background noise referred to as speech-in-noise difficulties. This condition is estimated to affect approximately 3% of the U.S. population, and is expected to grow significantly in the younger population because of exposure to excessive noise through widespread use of personal listening devices. Hearing aids provide limited benefit for speech-in-noise hearing problems and there is no FDA-approved drug treatment for this condition.

OTO-413 is a proprietary formulation of BDNF which is a naturally occurring protein involved in neuron growth and repair. Nonclinical studies by us and other research groups have demonstrated that local administration of BDNF repairs ribbon synapses damaged due to noise trauma or exposure to ototoxic chemicals and restores hearing function. We have initiated nonclinical studies and manufacturing for OTO-413 to support an IND Application, with a Phase 1/2 clinical trial expected to begin in hearing loss patients in the first half of 2019. The initial indication for OTO-413 will be patients with synaptopathy-related hearing loss that is characterized by speech-in-noise hearing difficulty.

OTO-5XX: Otoprotectant for Cisplatin-Induced Hearing Loss

Cisplatin and other platinum-based chemotherapeutic agents are routinely used in treating numerous tumor types with approximately 500,000 patients including 2,000 children treated each year in the United States according to market estimates. While use of platinum agents has contributed to improved patient survival, ototoxicity and associated permanent hearing loss is well documented in the clinical literature. In particular, hearing loss has been reported in up to 90% of children and young adults treated with platinum-based agents. This adversely affects speech and language development and has been associated with academic and social difficulties which can have a significant impact on patients and their families. At this time, there is no FDA-approved drug treatment to protect against platinum-based ototoxicity.

We established feasibility of conducting clinical trials in patients undergoing cisplatin chemotherapy through a small Phase 2 trial with OTIVIDEX in pediatric patients. We have identified a therapeutic target that offers a potentially higher level of otoprotection than steroids based on nonclinical proof-of-concept studies, and are evaluating molecules in this class. We expect to select a candidate for clinical development in the second half of 2018.

OTO-6XX: Hair Cell Regeneration for Severe Hearing Loss

Auditory hair cells are specialized sensory cells in the cochlea that convert sound vibrations into a signal that can be transmitted to the brain for interpretation as hearing. Unlike non-mammalian species such as birds that are able to naturally regenerate hair cells, a human is born with approximately 15,000 auditory hair cells per cochlea that do not regenerate. As a result, the loss of hair cells due to damage from excessive noise, physical trauma, exposure to ototoxic chemicals, or through the natural aging process is irreversible and results in permanent hearing loss. The treatment of hearing loss is a significant unmet need with approximately 360 million people worldwide having a disabling level of loss including approximately 6.6 million people in the U.S. with severe hearing loss. Hearing aids provide limited benefit and there are no FDA-approved drugs to treat hearing loss.

Considerable interest and attention has been focused by otology researchers over the past several decades for ways to regenerate auditory hair cells as an approach to treating severe hearing loss. This effort has included extensive research with non-mammalian species that do regenerate hair cells to identify pathways for therapeutic intervention. Targeting one of these pathways, we have demonstrated regeneration of hair cells in a nonclinical proof-of-concept model using a class of small molecules. We expect to select a candidate for clinical development in the second half of 2018.

OTIPRIO: Sustained-Exposure Topical Antibacterial for Otic Infections

OTIPRIO is a single-dose, physician-administered antibacterial that was approved by the FDA in December 2015 for the treatment of pediatric patients with bilateral otitis media with effusion undergoing TTP surgery and was recently approved for the treatment of patients with AOE. OTIPRIO is the only product approved by the FDA for use during TTP surgery and is the only single-dose topical antibacterial approved for the treatment of AOE. We have also completed a successful End-of-Phase 2 review with the FDA for OTIPRIO in patients with acute otitis media with tympanostomy tubes (AOMT). Based on FDA feedback, we believe that registration would require a single, sham controlled, pivotal Phase 3 trial enrolling approximately 200 pediatric patients with AOMT.

We provided promotional support for OTIPRIO using an internal sales force beginning in the first quarter of 2016 which continued into the fourth quarter of 2017. As of December 31, 2017, and 2016, net sales of OTIPRIO totaled $1.2 million and $0.7 million, respectively. In November 2017, we announced the discontinuation of promotional

support for OTIPRIO in order to significantly reduce operating expenses. OTIPRIO continues to be available for purchase by customers while we evaluate commercial partnering options for the product, including divestiture.

Our Proprietary Otic Drug Delivery Technologies

To overcome many of the limitations of delivering drugs to the ear, we have developed multiple proprietary formulation technologies designed to deliver drug that is retained in the ear for an extended period of time following a single local administration, which we refer to as “sustained-exposure.” One of these technologies utilizes a thermosensitive polymer called poloxamer which transitions from a liquid to a gel at body temperature. The polymer

vehicle is combined with drug microparticles to create a suspension that is retained in the ear for an extended period of time. This prolonged residence time provides high and sustained drug exposure.

Potential benefits of our drug delivery technologies for our product and product candidates include:

- Single local administration.
- High drug levels in the target location and minimal systemic exposure.
- Eliminates the need for the patient to remain in a prone position for an extended period of time.
- Simple, office-based administration by an ear, nose and throat physician (ENT).
- Avoids patient compliance concerns.

We have a broad patent portfolio of approximately 103 issued patents and allowed patent applications and at least 120 pending patent applications covering our product, product candidates and indications as well as other potential applications of our drug delivery technologies in major markets around the world.

Competition

The biopharmaceutical market is highly competitive. Successful competitors in the biopharmaceutical market must have the ability to effectively discover, develop, test and obtain regulatory approvals for products, as well as the ability to effectively commercialize, market and promote approved products, including communicating the effectiveness, safety and value of products to actual and prospective customers and medical staff. Numerous companies are engaged in the development, manufacture and marketing of biopharmaceutical products competitive with those that we are developing. Our potential competitors may have substantially greater manufacturing, financial, research and development, personnel and marketing resources than we have. Our competitors may also have more experience and expertise in obtaining marketing approvals from the FDA and other regulatory authorities. In addition to product development, testing, approval and promotion, other competitive factors in the biopharmaceutical industry include industry consolidation, product quality and price, product technology, reputation, customer service and access to technical information. As a result, our competitors may be able to develop competing or superior technologies and processes, and compete more aggressively and sustain that competition over a longer period of time than we could. Our technologies and products may be rendered obsolete or uneconomical by technological advances or entirely different approaches developed by one or more of our competitors. As more companies develop new intellectual property in our market, the possibility of a competitor acquiring patent or other rights that may limit our products or potential products increases, which could lead to litigation.

Any product candidates that we successfully develop and commercialize will compete with existing treatments, including unapproved and off-label drug alternatives that are currently utilized by physicians to treat the indications for which we seek approval, as well as new treatments that may become available in the future.

OTIPRIO

Antibiotic ear drops are currently the primary treatment option for use during TTP surgery even though no ear drop product has been approved by the FDA for this indication. Multiple ear drops are approved and marketed for use in treating patients with AOE and AOMT. Marketed antibiotic ear drops include CIPRODEXâ Otic from Alcon, a Novartis company, and Otovelâ from Arbor Pharmaceuticals, LLC. The key competitive factors affecting the success of OTIPRIO are likely to be its efficacy, safety, tolerability, dosing regimen, route of administration, convenience and price, and the availability of coverage and adequate reimbursement from government and other third-party payors.

OTIVIDEX

There are no drugs currently approved by the FDA for the treatment of Ménière's disease. Current treatments commonly used for Ménière's disease in the United States include observance of a low-salt diet and off-label use of diuretics, oral steroids, and repeat IT injections of steroid solution. Patients who are unresponsive to treatment may

resort to surgical or chemical ablation, which can cause irreversible hearing loss. We are aware that Sound Pharmaceuticals initiated a Phase 2b clinical trial with SP-1005, Synphora AB initiated a Phase 2 clinical trial with an IT formulation of latanoprost, and Auris Medical Holding AG is developing AM-125, a nasal formulation of betahistine, for the treatment of vertigo disorders including Ménière's disease.

OTO-313

There are no drugs currently approved by the FDA for the treatment of tinnitus. Current treatments for tinnitus include the use of audio masking devices, such as white noise machines, hearing aids, cognitive behavioral therapy, and the off-label administration of antidepressants, anti-anxiety medications, and steroids. We are aware of other companies developing potential pharmaceutical treatments for tinnitus, including Auris Medical Holding AG, which is conducting a Phase 3 clinical program evaluating repeat IT injections of Keyzilenâ (formerly AM-101) in patients with tinnitus. The first Phase 3 trial failed to achieve the primary endpoint and a second Phase 3 trial is ongoing. We are also aware that Autifony Therapeutics terminated a Phase 2 trial for AUT00063 in tinnitus patients following a planned interim analysis, Merz Pharmaceuticals GmbH suspended development of oral neramexane for chronic tinnitus while its partner in Japan, Kyorin Pharmaceutical Co., continues with a Phase 2 clinical trial for tinnitus, and Novartis AG completed a Phase 2 clinical trial for chronic tinnitus.

Hearing Loss Programs

There are no drugs currently approved by the FDA for the treatment of hearing loss. Oral steroids and repeat IT steroid injections are often used for the treatment of sudden sensorineural hearing loss (SSNHL), which is a rapidly emergent form of hearing loss. Hearing aids are used by a subset of patients with hearing loss and a limited number of patients with severe hearing loss are treated with cochlear implants. We are aware of a number of companies in clinical development with potential pharmaceutical treatments for various hearing loss indications, including Auris Medical Holding AG, which has completed a Phase 3 trial for AM-111 in SSNHL, Fennec Pharmaceuticals which has completed two Phase 3 trials for PEDMARKä in CIHL, Metarmor, which is conducting a Phase 3 trial with D-MET in noise-induced hearing loss (NIHL), Strekin AG, which is conducting a Phase 2 trial with STR001 in patients undergoing cochlear implantation and intends to initiate a Phase 3 trial with STR001 in SSNHL, Sound Pharmaceuticals, which has completed a Phase 2 trial with SPI-1005 in patients with NIHL and is initiating trials for aminoglycoside-induced hearing loss and CIHL, Sensorion, which is planning to initiate a Phase 2 trial with SENS-401 in SSNHL and CIHL, Frequency Therapeutics, which has completed a Phase 1 safety trial in patients with severe to profound hearing loss, Otologic Pharmaceutics, which has completed a Phase 1 trial with NHPN-010, and Oricula Therapeutics, which has clearance to initiate a Phase 1 trial with ORC-13661.

Sales and Marketing

We commercialized OTIPRIO using an internal sales force beginning in the first quarter of 2016 and continued promotional support into the fourth quarter of 2017. In November 2017, we announced the discontinuation of promotional support for OTIPRIO in order to significantly reduce operating expenses. OTIPRIO continues to be available for purchase by customers while we evaluate commercial partnering options for the product, including divestiture.

We plan to evaluate whether to commercialize our product candidates on our own or in collaboration with partners in the United States and for markets outside the United States.

Third-Party Payor Coverage and Reimbursement

Sales of pharmaceutical products depend in significant part on the availability of coverage and adequate reimbursement by third-party payors, such as state and federal governments, including Medicare and Medicaid, and commercial insurers. Decisions regarding the extent of coverage and amount of reimbursement to be provided for our products will most likely be made on a plan-by-plan basis.

OTIPRIO

OTIPRIO is billable as a physician-administered drug in the United States using the J Code that was assigned to the product by the Centers for Medicare and Medicaid Services (CMS) and became effective as of January 1,

2017. The Wholesale Acquisition Cost for OTIPRIO is $283.20 per vial. A single vial of OTIPRIO is sufficient for treating a patient during TTP surgery or for the treatment of AOE.

OTIVIDEX, OTO-313 and OTO-413

If approved by the FDA, we intend to apply to CMS for unique J Codes for OTIVIDEX, OTO-313 and OTO-413 to support reimbursement in the physician office setting. If a J Code is granted and accepted by payors then each product is expected to be reimbursed according to its average selling price and in addition to the fee the physician receives for performing the IT injection procedure itself.

Manufacturing

We currently contract with third parties for the manufacture, testing and storage of our product and product candidates and intend to continue to do so in the future. We do not own and have no plans to build our own clinical or commercial manufacturing capabilities. The use of contracted manufacturing is relatively cost-efficient and has eliminated the need for our direct investment in manufacturing facilities. Because we rely on contract manufacturers, we employ personnel with extensive technical, manufacturing, analytical and quality experience to oversee contract manufacturing and testing activities, and to compile manufacturing and quality information for our regulatory submissions.

Manufacturing is subject to extensive regulations that impose various procedural and documentation requirements, and which govern record keeping, manufacturing processes and controls, personnel, quality control and quality assurance, among others. Our systems and our contractors are required to be in compliance with these regulations, and this is assessed regularly through monitoring of performance and a formal audit program. To date, our third-party manufacturers have met our manufacturing requirements for clinical trials and our third-party manufacturer for OTIPRIO successfully passed a pre-approval inspection conducted by the FDA. We expect third-party manufacturers to be capable of providing sufficient quantities of our product and product candidates to meet anticipated commercial demands. We believe that there are alternate sources of raw material supply and finished goods manufacturing that can satisfy our requirements, although we cannot be certain that transitioning to such vendors, if necessary, would not result in significant delay or material additional costs.

Poloxamer 407

The basis for the formulation of our product and certain of our product candidates is P407, a thermosensitive polymer. We currently purchase P407 from a single supplier on a purchase-order basis under a supply agreement. Although P407 is available from other sources, changing suppliers could disrupt our supply chain. We believe that we can effectively manage the risk of supply chain disruption by purchasing and storing quantities of P407 sufficient for our clinical and commercial requirements.

OTIPRIO

OTIPRIO is a suspension containing the antibiotic ciprofloxacin and P407. The raw materials needed for the manufacture of OTIPRIO are commercially available from multiple sources. We have qualified two sources of ciprofloxacin and have a supply agreement in place with one of the vendors. We currently use a single third-party contract manufacturer, Siegfried Irvine, located in Irvine, California, to produce OTIPRIO, and we believe this manufacturer can satisfy our commercial requirements as specified under a commercial supply agreement executed with this manufacturer.

OTIVIDEX

OTIVIDEX is a suspension containing the steroid dexamethasone and P407. We currently purchase dexamethasone from a single supplier on a purchase-order basis and we do not have a long-term supply agreement. Although dexamethasone is commercially available from other sources, we do not anticipate needing an alternative supplier. We believe that we can effectively manage the risk of supply chain disruption by purchasing and storing quantities of dexamethasone sufficient for our clinical, and, if OTIVIDEX is approved for marketing by the

applicable regulatory authorities, our commercial requirements. We currently use two third-party contract manufacturers to produce OTIVIDEX that we believe can satisfy our clinical requirements. We are currently evaluating our supply chain for the commercial manufacture of OTIVIDEX.

OTO-313

OTO-313 is a formulation containing gacyclidine. We currently purchase gacyclidine from a single supplier on a purchase-order basis and we do not have a long-term supply agreement. We currently use one third-party contract manufacturer to produce OTO-313 that we believe can satisfy our clinical requirements.

OTO-413

OTO-413 is a formulation containing BDNF. We currently purchase BDNF from a single supplier on a purchase-order basis and we do not have a long-term supply agreement. We expect to use one third-party contract manufacturer to produce OTO-413 that we believe can satisfy our clinical requirements.

Intellectual Property

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

As for the product candidates we develop and plan to commercialize, as a normal course of business, we intend to pursue composition and therapeutic use patents, as well as novel indications for our product candidates. We also seek patent protection with respect to novel discoveries, including new active agent, delivery vehicle and delivery target applications. We have also pursued patents with respect to our proprietary manufacturing processes. We have sought and plan to continue to seek patent protection, either alone or jointly with our collaborators, as our collaboration agreements may dictate.

It is possible that our current patents, or patents which we may later acquire, may be successfully challenged or invalidated in whole or in part. Nevertheless, we are not aware of any issued patents that we believe would prevent us from marketing OTIPRIO or our product candidates. It is also possible that we may not obtain issued patents from our pending patent applications or other inventions we seek to protect. Due to uncertainties inherent in prosecuting patent applications, patent applications are sometimes rejected and we subsequently abandon them. It is also possible that we may develop proprietary products or technologies in the future that are not patentable or that the patents of others will limit or altogether preclude our ability to do business. In addition, any patent issued to us may provide us with little or no competitive advantage, in which case we may abandon such patent or license it to another entity. For more information, please see the section entitled “Risk Factors—Risks Related to Our Intellectual Property.”

Our patent estate includes patents and applications with claims directed to OTIPRIO, and our OTIVIDEX, OTO-313, OTO-413, and other product candidates. Our patent estate also provides patents and applications with claims directed to a broad range of other active agents as potential future product candidates that are delivered using our proprietary technologies. Our patent estate, on a worldwide basis, includes approximately 103 issued patents and allowed patent applications, and at least 120 pending patent applications with claims relating to our OTIPRIO, OTIVIDEX, OTO-313, OTO-413, other product candidates, future product candidates, manufacturing processes and alternative

otic delivery technologies.

For OTIPRIO, we co-own a patent family with The Regents of the University of California (UC) that is directed to the composition and therapeutic use of OTIPRIO. Through an exclusive license agreement, we have acquired UC's rights in this patent family. This family includes four issued U.S. patents and three pending U.S.

applications. The latest expiry date of the U.S. patents, without extensions, is April 2030, and the first three issued U.S. patents have been Orange Book (OB) listed. The fourth issued patent is expected to be OB listable for AOE. The fifth issued patent is expected to be OB listable for AOMT, if approved by FDA. Any future U.S. patents issuing from the related applications and directed to OTIPRIO are also expected to be OB listable. This family also includes issued patents or allowed applications in Australia, Canada, Europe, India, Israel, Japan, Korea, Mexico, Philippines, Russia, Singapore, South Africa and Taiwan; and pending applications in Argentina, Brazil, China, Jordan, Pakistan, Thailand, Uruguay and Venezuela. Divisional patent applications have been filed in select countries of this family. In addition, we solely own a patent family directed to certain therapeutic uses of OTIPRIO, which includes an issued U.S. patent that has been submitted for OB listing and can extend patent protection of OTIPRIO to August 2034; and a pending application that, upon issuance, is expected to be OB listable. Outside of U.S., this patent family includes pending applications in Australia, Brazil, Canada, China, Eurasia, Europe, Japan, Korea, and Mexico. Furthermore, we solely own a patent family directed to OTIPRIO and its manufacturing methods, which includes an issued U.S. patent that has been OB listed and extends patent protection of OTIPRIO to July 2035; and another issued U.S. patent that has been submitted for OB listing. Outside of U.S., this patent family includes pending applications in Australia, Canada, China, Europe, Japan, and Korea. Finally, we solely own a patent family directed to the packaged OTIPRIO product, and two patent families directed to AOE and AOMT.

For OTIVIDEX, we co-own a patent family with UC directed to the composition and therapeutic use of OTIVIDEX. Through an exclusive license agreement, we have acquired UC's rights in this patent family. This family includes seven issued U.S. patents and one pending U.S. application. The latest expiry date of the U.S. patents, without extensions, is September 2029, and these patents and any future U.S. patent issuing from the related applications are expected to be OB listable. This family also includes issued patents or allowed applications in Australia, Canada, Chile, China, Europe, Hong Kong, India, Israel, Japan, Korea, Malaysia, Mexico, Peru, Philippines, Russia, Singapore, South Africa, Taiwan, UK, and Vietnam; and pending applications in Argentina, Brazil, Indonesia, Jordan, Pakistan, Thailand, Uruguay, and Venezuela. Divisional patent applications have been filed in select countries for this family. In addition, we solely own a patent family directed to additional therapeutic uses of OTIVIDEX, including prevention of chemotherapeutic drug-induced ototoxicity. Finally, we solely own an issued U.S. patent directed to manufacturing methods of OTIVIDEX. The expiry date of this U.S. patent, without extensions, is April 2030.

For OTO-313, we solely own a patent family directed to, among other things, the composition and therapeutic use of OTO-313. This family includes one pending U.S. application and one PCT application. Any future U.S. and foreign patents issuing from those applications are expected to have an expiry date of June 2037. In addition, we have licensed from Durect a patent family directed to the therapeutic use of OTO-313. This family includes one issued U.S. patent and one issued Japanese patent. The expiry date of the U.S. patent, without extension, is June 2024, and the patent is expected to be OB listable.

For OTO-413, we co-own a patent family with UC that may be related to certain aspects of the composition and therapeutic use of OTO-413. Through an exclusive license agreement, we have acquired UC's rights in this patent family. Any future U.S. or foreign patents issuing from this patent family and directed to OTO-413 are expected to have an expiry date of April 2029. In addition, we solely own two patent families directed to certain aspects of the composition and therapeutic use of OTO-413. Any future U.S. or foreign patents issuing from those patent families and directed to OTO-413 are expected to have an expiry date of June 2037 and January 2039, respectively.

For our future product candidates, we co-own eight other patent families with UC directed to a broad range of other active agents, including but not limited to, anti-TNF agents, auris pressure modulators, CNS modulators, cytotoxic agents, anti-apoptotic agents, bone-remodeling modulators, free radical modulators and ion channel modulators. As above, we have acquired, though an exclusive license, UC's rights in those co-owned families. Furthermore, to strengthen our protection against potential design-around, we solely own two patent families directed to alternative formulations. Finally, we have acquired from IncuMed LLC, an affiliate of the NeuroSystec Corporation, patent

families directed to formulations or devices that deliver active agents, such as the active agent of OTO-313, into the ear for treatment of otic diseases through alternative delivery technologies. We will continue to pursue additional patent protection as well as take appropriate measures to obtain and maintain proprietary protection for our innovative technologies.

Individual patents extend for varying periods depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued for regularly filed applications in the United States are effective for 20 years from the earliest effective filing date. In addition, in certain instances, a patent term can be extended to recapture a portion of the U.S. Patent and Trademark Office (USPTO) delay in issuing the patent as well as a portion of the term effectively lost as a result of the FDA regulatory review period. However, as to the FDA component, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest effective filing date. In addition to the patents and allowed applications described in the preceding paragraphs, our pending patent applications related to our product candidates, if issued, are expected to expire on dates ranging from 2029 to 2032. However, the actual protection afforded by a patent varies on a product by product basis, from country to country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

In addition to patents, we have obtained trademark registration for “OTIPRIO” in the United States, Europe, Japan, Korea, and New Zealand, and have pending trademark application for “OTIPRIO” in Australia, Canada, and China. Furthermore, we rely upon trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our commercial partners, collaborators, employees and consultants and invention assignment agreements with our employees. We also have confidentiality agreements or invention assignment agreements with our commercial partners and selected consultants. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with a third party. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our commercial partners, collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. For more information, please see the section entitled “Risk Factors—Risks Related to Our Intellectual Property.”

Our commercial success will also depend in part on not infringing upon the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, or our drugs or processes, obtain licenses or cease certain activities. Our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our future products may have a material adverse impact on us. If third parties prepare and file patent applications in the United States that also claim technology to which we have rights, we may have to participate in interference proceedings in the USPTO, to determine priority of invention. Although it is not expected to be relevant to our product or any of our product candidates, on April 17, 2015, we filed a request for interference between one of our U.S. pending applications and a U.S. pending application that appears to be controlled by Auris Medical AG (Auris). On July 20, 2015, we received notice from the USPTO that the Patent Trial and Appeal Board (PTAB) declared an interference between our pending application and the Auris patent (issued as U.S. Patent No. 9,066,865 on June 30, 2015). On January 26, 2017, the PTAB determined that all of our patent claims and all but one of the Auris patent claims are not patentable. In addition, the PTAB determined that the written description supporting Auris’s single claim is as of Auris’s filing date of 2014 rather than the 2005 dated argued by Auris. This interference decision does not involve issued U.S. patents covering our product or product candidates. We filed a Notice of Appeal on March 27, 2017, in which we asked the Federal Circuit to reverse PTAB’s decision that our claims are not patentable and that Auris’s single claim is. On April 5, 2017, Auris filed a Notice of Cross-Appeal to ask the Federal Circuit to reverse PTAB’s decision that Auris’s other claims are not patentable. The appeal proceedings are ongoing. We continue to monitor patent applications filed and being protected by Auris, in case we may need to consider similar or other actions. For more information, please see

the section entitled “Risk Factors—Risks Related to Our Intellectual Property.”

License and Other Agreements

The Regents of the University of California

In November 2008, we entered into an exclusive license agreement with UC that was subsequently amended in January 2010, June 2010, and November 2012. Under the license agreement, UC granted us an exclusive license under UC's rights to patents and applications that are co-developed and co-owned with us (see above regarding our patent estate) for the treatment of human otic diseases. As such, we have acquired the entire commercial rights in those patents and applications that cover OTIPRIO and OTIVIDEX, and may apply to other product candidates we develop. Under the agreement, UC reserved the right to use the patents and applications for its and other nonprofit institutions' research and educational purposes.

Under our agreement with UC, we are obligated to diligently proceed with the development, manufacture and commercialization of licensed products. If we do not satisfy our diligence obligations, UC may either terminate the agreement or convert our license to a non-exclusive license. In addition, we are responsible for diligently prosecuting and maintaining the licensed patents, at our own expense; provided that if we decide to abandon a licensed patent, UC may elect to continue prosecution and maintenance of such patent at its own expense. UC has the first right to prosecute and control any action for infringement of the patents licensed to us under our agreement with UC; provided that if UC does not initiate an enforcement action against a potential infringer within the time limits specified in the agreement, we have the right to do so ourselves.

Our financial obligations under the license agreement include annual license maintenance payments until we commercialize the first product covered under the license agreement, development and regulatory milestone payments of up to $2.7 million per licensed product, of which $1.9 million has been paid for OTIPRIO, $0.8 million has been paid for OTIVIDEX, and $0.1 million has been paid for OTO-311 (but such milestone payments are reduced by 75% for any orphan indication product), and a low single-digit royalty on net sales by us or our affiliates of licensed products. In addition, for each sublicense we grant we are obligated to pay UC a fixed percentage of all royalties as well as a sliding scale percentage of non-royalty sublicense fees received by us under such sublicense, with such percentage depending on the licensed product's stage of development when sublicensed to such third party. We have the right to offset a certain amount of third-party royalties, milestone fees or sublicense fees against the foregoing financial obligations, provided such third-party royalties or fees are paid by us in consideration for intellectual property rights necessary to commercialize a licensed product.

Unless earlier terminated, the agreement will continue in effect until expiration of the longest-lived patent licensed to us thereunder. UC may terminate the license agreement for our uncured breach, or if a claim challenging the validity of the licensed patents is filed by or on behalf of us. We have the right to terminate this agreement for any reason at any time upon prior notice to UC. The termination of our license agreement with UC may affect a portion of our patent portfolio for OTIPRIO and OTIVIDEX, as well as certain other product candidates we may develop. For more information, please see the section entitled "Risk Factors—Risks Related to our Intellectual Property."

DURECT Corporation

In April 2013, we entered into an exclusive license agreement with Durect as a part of an asset transfer agreement between us and IncuMed LLC, an affiliate of the NeuroSystec Corporation. Under this license agreement, Durect granted us an exclusive (even as to Durect), worldwide, royalty-bearing license under Durect's rights to certain patents and applications that cover our OTO-313 product candidate, as well as certain related know-how. Included within the rights licensed from Durect is a sublicense from the Institut National de la Sante et de la Recherche Medicale (INSERM) with respect to INSERM's ownership interest in certain patents and patent applications owned jointly by INSERM and Durect.

We are obligated to use commercially reasonable efforts to develop and commercialize licensed products containing the active ingredient gacyclidine, and in the event, we do not satisfy this obligation following an opportunity to cure, Durect may elect to either terminate the agreement or convert our license to a non-exclusive license. In addition, we are responsible for prosecuting and maintaining the licensed patents, at our own expense; provided that if we decide to abandon a licensed patent, Durect may elect to continue prosecution and maintenance

of such patent at its own expense. We have the first right, but not obligation, to prosecute and control any action for infringement of the patents licensed to us under our agreement with Durect.

We are also subject to certain financial obligations under the license agreement. We are obligated to make one-time development milestone payments of up to $2.3 million for the first licensed product. Upon commercializing a licensed product, we are obligated to pay Durect tiered low single-digit royalties on annual net sales by us or our affiliates or sublicensees of the licensed products, and we have the right to offset a certain amount of third-party license fees or royalties against such royalty payments to Durect, provided such third-party fees or royalties are paid by us in connection with patent rights necessary to sell a licensed product containing the active ingredient gacyclidine. In addition, each sublicense we grant to a third party is subject to payment to Durect of a low double-digit percentage of all non-royalty payments we receive under such sublicense. Additionally, we are also obligated to pay INSERM, on behalf of Durect, a low single-digit royalty payment on net sales by us or our affiliates or sublicensees upon commercialization of the licensed product. The foregoing royalty payment obligation to Durect would continue on a product-by-product and country-by-country basis until expiration or determination of invalidity of the last valid claim within the licensed patents that cover the licensed product, and the payment obligation to INSERM would continue so long as Durect's license from INSERM remains in effect.

Unless earlier terminated, the agreement will continue in effect until expiration of all our royalty payment obligations thereunder. Durect may terminate the license agreement for our uncured material breach, and either party may terminate the agreement upon written notice in the event of insolvency or bankruptcy of the other party. We have the right to terminate this agreement for any reason at any time upon prior notice to Durect. The termination of our license agreement with Durect would affect a portion of our patent portfolio for OTO-313. For more information, please see the section entitled "Risk Factors—Risks Related to our Intellectual Property."

Asset Transfer Agreement

In April 2013, we entered into an asset transfer agreement with IncuMed, LLC, an affiliate of NeuroSystec Corporation, pursuant to which we acquired assets and patent rights related to gacyclidine. Pursuant to the asset transfer agreement, we made a one-time payment of $0.2 million and we are obligated to make certain one-time milestone payments in connection with the development and commercialization of products containing the active ingredient gacyclidine, up to a maximum of $5.3 million.

Government Regulation

Government authorities in the United States (at the federal, state and local level) and in other countries extensively regulate, among other things, the research, development, testing, quality control, manufacture, packaging, storage, recordkeeping, approval, labeling, advertising, promotion, distribution, marketing, import and export of pharmaceutical products such as those we are developing. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations, require the expenditure of substantial time and financial resources. Our product candidates must be approved by the FDA before they may be legally marketed in the United States and by the appropriate foreign regulatory agency before they may be legally marketed in foreign countries. Generally, our activities in other countries will be subject to regulation that is similar in nature and scope as that imposed in the United States, although there can be important differences. Additionally, some significant aspects of regulation in Europe are addressed in a centralized way, but country-specific regulation remains essential in many respects.

U.S. Drug Approval Process

In the United States, the FDA regulates drugs under the federal Food, Drug, and Cosmetic Act (FDCA) and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending NDAs, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal

penalties. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of nonclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's current good laboratory practice (cGLP) regulations;
- submission to the FDA of an IND which must become effective before clinical trials may begin;
- approval by an independent institutional review board (IRB) at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled clinical trials in accordance with current good clinical practices (cGCP) to establish the safety and efficacy of the proposed drug or biological product for each indication;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMP, and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and
- FDA review and approval of the NDA.

Nonclinical Studies

Nonclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess its potential safety and efficacy. An IND sponsor must submit the results of the nonclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some nonclinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to patients under the supervision of qualified investigators in accordance with cGCP requirements, which include the requirement that all research patients provide their informed consent (assent, if applicable) in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness 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. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health (NIH) for public dissemination on their ClinicalTrials.gov website.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- Phase 1: The drug is initially introduced into healthy human patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.
- Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA may impose a partial or full clinical hold or the sponsor may suspend or terminate a clinical trial or development at any time on various grounds, including a finding that the research patients are being exposed to an unacceptable health risk.

Development, or the aspects of development, that are subject to clinical hold may not continue until the sponsor has satisfied FDA requirements for information and has been notified that the hold is being removed. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

The NDA Approval Process

Assuming successful completion of the required clinical testing, the results of the nonclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. Under the Prescription Drug User Fee Act (PDUFA) guidelines that are currently in effect, the FDA has a goal of ten months from the date of the FDA's filing of a standard non-priority NDA to review and act on the submission.

The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity. The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. 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.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured, which is not under the control of the product sponsor. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure

consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with cGCP.

The FDA also may require submission of a risk evaluation and mitigation strategy (REMS) plan to mitigate any identified or suspected serious risks. The REMS plan could include medication guides, physician communication plans, assessment plans and elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools.

The testing and approval process requires substantial time, effort and financial resources, and each may take several years to complete. Data obtained from clinical activities are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all.

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new products that meet certain criteria. Specifically, new products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. Unique to a Fast Track product, the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA. Our Fast Track Designation for OTIVIDEX may not result in faster development or approval, if at all.

If the FDA's evaluation of the NDA and inspection of the manufacturing facilities are favorable, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or nonclinical testing in order for FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

The Section 505(b)(2) NDA

For modifications to products previously approved by the FDA, an applicant may file an NDA under Section 505(b)(2) of the FDCA. This section permits the submission of an NDA where some or all of the data required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. Under this section, an applicant may rely on the FDA's findings of safety and effectiveness in approval of another NDA or on studies published in the scientific literature. The applicant may be required to conduct additional studies or provide additional information to fully demonstrate the safety and effectiveness of its modifications to the approved product.

Upon approval of an NDA, the FDA lists the product in a publication entitled “Approved Drug Products with Therapeutic Equivalence Evaluations,” which is commonly known as the “Orange Book.” FDA also lists in the Orange Book patents identified by the NDA applicant as claiming the drug or an approved method of using the drug. Any applicant who submits a Section 505(b)(2) NDA must certify to the FDA with regard to each relevant patent that either (1) no patent information has been submitted to the FDA; (2) the patent has expired; (3) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (4) the patent is

invalid or will not be infringed upon by the manufacture, use or sale of the drug product for which the Section 505(b)(2) NDA is submitted. The last certification is known as a Paragraph IV certification. A notice of Paragraph IV certification must be provided to each owner of the patent that is the subject of the certification and to the holder of the approved NDA to which the Section 505(b)(2) NDA refers. If the NDA holder submits the patent information to the FDA prior to submission of the Section 505(b)(2) application and the NDA holder or patent owner(s) sues the Section 505(b)(2) applicant for infringement within 45 days of its receipt of the certification notice, the FDA is prevented from approving that Section 505(b)(2) application until the earlier of 30 months from the receipt of the notice of the Paragraph IV certification, the expiration of the patent or such shorter or longer period as may be ordered by a court. This prohibition is generally referred to as the 30-month stay. A Section 505(b)(2) applicant that is sued for infringement may file a counterclaim to challenge the listing of the patent or information submitted to FDA about the patent. If we file a Paragraph IV certification with any Section 505(b)(2) application, we cannot assure you that our application will not be significantly delayed as a result of costly patent litigation.

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.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product’s safety and effectiveness after commercialization.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies to determine compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often 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 the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend significant time, money and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the 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 or other restrictions under a REMS program. Other potential consequences include, among other things:

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

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

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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, although doctors may prescribe drugs for off-label purposes.

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.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act (PDMA) which regulates the distribution of drug and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states.

Hatch-Waxman Exclusivity

Market and data exclusivity provisions under the Federal Food, Drug, and Cosmetic Act (FFDCA) can delay the submission or the approval of certain applications for competing products. The FFDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an Abbreviated New Drug Application (ANDA) or a Section 505(b)(2) NDA submitted by another company that references the previously approved drug. However, an ANDA or Section 505(b)(2) NDA may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FFDCA also provides three years of marketing exclusivity for an NDA, Section 505(b)(2) NDA or supplement to an existing NDA or Section 505(b)(2) NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant, are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages, strengths or dosage forms of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and, as a general matter, does not prohibit the FDA from approving ANDAs or Section 505(b)(2) NDAs for generic versions of the original, unmodified drug product. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the nonclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

New Legislation and Regulations

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the testing, approval, manufacturing and marketing of products regulated by the FDA. In addition to new legislation, FDA regulations and policies are often revised or interpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether further legislative changes will be enacted or FDA regulations, guidance, policies or interpretations will be changed, or what the impact of such changes, if any, may be.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any drug products for which we may obtain regulatory approval. Sales of any of our product candidates, if approved, will depend, in part, on the extent to which the costs of the products will be covered by third-party payors, including government health programs such as Medicare and Medicaid, commercial health insurers and managed care organizations. The process for determining whether a third-party payor will provide coverage for a drug product typically is separate from the process for setting the price of a drug product or for establishing the reimbursement rate that a payor will pay for the drug product once

coverage is approved. Third-party payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the approved drugs for a particular indication.

In order to secure 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 the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Whether or not we conduct such studies, our product candidates may not be considered medically necessary or cost-effective. A third-party payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage, and adequate reimbursement, for the product. Third-party reimbursement may not be sufficient to enable us to maintain price levels high enough to realize an appropriate return on our investment in product development.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drugs have been a focus in this effort. Third-party payors are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost-effectiveness of drug products and medical services and questioning safety and efficacy. If these third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after FDA approval or, if they do, the level of payment may not be sufficient to allow us to sell our 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. Adoption of such controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals such as our drug product candidates and could adversely affect our net revenue and results.

Pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies. For example, the EU provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU member states may approve a specific price for a drug product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products, but monitor and control company profits. The downward pressure on healthcare costs in general, particularly prescription drugs, has become 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 competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements for any of our products.

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, emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on drug pricing. Coverage policies, third-party reimbursement rates and drug pricing regulation may change at any time. In particular, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, which we collectively refer to as the Affordable Care Act (ACA), contains provisions that have the potential to substantially change healthcare delivery and financing, including impacting the profitability of drugs. For example, the ACA revised the methodology by which rebates owed by manufacturers to the state and federal government for covered outpatient drugs under the Medicaid Drug Rebate Program, extended the Medicaid Drug Rebate Program to utilization of covered drugs dispensed to individuals enrolled in Medicaid managed care organizations and subjected manufacturers to new annual fees and taxes for certain branded prescription drugs. 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.

Healthcare Law and Regulation

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescribing of any product candidates for which we may obtain marketing approval. Our business operations and arrangements with investigators, healthcare professionals, consultants, third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws. These laws may constrain the business or

financial arrangements and relationships through which we research, manufacture, market, promote, sell and distribute our products that obtain marketing approval. Restrictions under applicable federal and state healthcare laws, include, but are not limited to, the following:

- the federal healthcare Anti-Kickback Statute prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal false claims laws and civil monetary penalties law impose penalties and provide for civil whistleblower or qui tam actions against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false or fraudulent or making a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) among other things, imposes criminal liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without proper written authorization;
- the federal transparency requirements under the ACA requires manufacturers of drugs, devices, biologicals and medical supplies to annually report to the Centers for Medicare & Medicaid Services (CMS) an agency within the U.S. Department of Health and Human Services (HHS) information related to payments and other transfers of value provided to physicians and teaching hospitals and certain ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws, such as state anti-kickback and false claims laws, that may apply to our business operations, including our sales or marketing arrangements, and claims involving healthcare items or services reimbursed by governmental third-party payors, and in some instances, also such claims reimbursed by non-governmental third-party payors, including private insurers.

Similar to the federal law, certain states also have adopted marketing and/or transparency laws relevant to manufacturers, some of which are broader in scope. Other states impose restrictions on manufacturers marketing practices and require tracking and reporting of gifts, compensation, and other remuneration to healthcare professionals and entities. 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. For instance, EU data protection law, in particular the new EU General Data Protection Regulation (the GDPR), which will become fully applicable on May 25, 2018, includes, among other things, requirements for individuals' consent, restrictions on the processing of health data, notice obligations, restrictions for the transfer of personal data outside of the EU, security and confidentiality obligations, and significant fines in case of violation.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws 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. 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 administrative, civil, and/or criminal penalties, damages, fines, disgorgement, individual imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business is found to be not in compliance with applicable

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laws, they may be subject to administrative, civil, and/or criminal sanctions, including exclusions from government funded healthcare programs.

Foreign Regulation

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. The cost of establishing a regulatory compliance system for numerous varying jurisdictions can be very significant. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable foreign regulatory authorities before we can commence clinical trials or marketing of the product in foreign countries and jurisdictions. Although many of the issues discussed above with respect to the United States apply similarly in the context of the EU, 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.

The U.S. Foreign Corrupt Practices Act and Other Anti-Corruption Laws

We may be subject to a variety of domestic and foreign anti-corruption laws with respect to our regulatory compliance efforts and operations. The U.S. Foreign Corrupt Practices Act, commonly known as the FCPA, is a criminal statute that prohibits an individual or business from paying, offering, promising or authorizing the provision of money (such as a bribe or kickback) or anything else of value (such as an improper gift, hospitality, or favor), directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision in order to assist the individual or business in obtaining, retaining, or directing business or other advantages (such as favorable regulatory rulings). The FCPA also obligates companies with securities listed in the United States to comply with certain accounting provisions. Those provisions require a company such as ours to (i) maintain books and records that accurately and fairly reflect all transactions, expenses, and asset dispositions, and (ii) devise and maintain an adequate system of internal accounting controls sufficient to provide reasonable assurances that transactions are properly authorized, executed and recorded. The FCPA is subject to broad interpretation by the U.S. government. The past decade has seen a significant increase in enforcement activity. In addition to the FCPA, there are a number of other federal and state anti-corruption laws to which we may be subject, including, the U.S. domestic bribery statute contained in 18 USC § 201 (which prohibits bribing U.S. government officials) and the U.S. Travel Act (which in some instances addresses private-sector or commercial bribery both within and outside the United States). Also, a number of the countries in which we conduct activities have their own domestic and international anti-corruption laws, such as the UK Bribery Act 2010. There have been cases where companies have faced multi-jurisdictional liability under the FCPA and the anti-corruption laws of other countries for the same illegal act.

We can be held liable under the FCPA and other anti-corruption laws for the illegal activities of our employees, representatives, contractors, partners, agents, subsidiaries, or affiliates, even if we did not explicitly authorize such activity. Although we will seek to comply with anti-corruption laws, there can be no assurance that all of our employees, representatives, contractors, partners, agents, subsidiaries or affiliates will comply with these laws at all times. Noncompliance with these laws could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension and/or debarment from contracting with certain governments or other persons, the loss of export privileges, reputational harm, adverse media coverage, and other collateral consequences. In addition, our directors, officers, employees, and other representatives who engage in violations of the FCPA and

certain other anti-corruption statutes may face imprisonment, fines, and penalties. If any subpoenas or investigations are launched, or governmental or other sanctions are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, results of operations and financial condition could be materially harmed. In addition, responding to any action will likely result in a materially significant diversion of management's attention and resources and significant defense costs and other professional fees. Enforcement actions and sanctions could further harm our business, results of operations, and financial condition.

Research and Development

We recognized $42.7 million, $60.7 million and $38.8 million in research and development expenses in the years ended December 31, 2017, 2016 and 2015, respectively. The significant majority of these research and development expenses have related to our development of OTIPRIO and OTIVIDEX.

Geographic Information

During 2017, 2016 and 2015, substantially all of our long-lived assets were located within the United States.

Financial Information about Segments

We manage our operations as a single reportable segment for the purposes of assessing performance and making operating decisions. See Note 2 – "Summary of Significant Accounting Policies" – in the notes to the financial statements included elsewhere in this Annual Report on Form 10-K.

Employees

As of December 31, 2017, we had 53 full-time employees. None of our employees is represented by a labor union or covered by collective bargaining agreements, and we believe our relationship with our employees is good. In November 2017, we announced the elimination of employment positions in connection with our discontinuation of promotional support for OTIPRIO in order to significantly reduce operating expenses related to the product.

Corporate Information

We were incorporated in Delaware on May 6, 2008. Our principal executive offices are located at 4796 Executive Drive, San Diego, CA 92121. Our telephone number is (619) 323-2200. Our website address is www.otonomy.com.

This Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and any amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, (Exchange Act) are available (free of charge) on our website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission (SEC).

Information contained on, or that can be accessed through, our website or social media sites does not constitute part of this Annual Report on Form 10-K or any other report or document we file with the SEC, and any references to our website and social media sites are intended to be inactive textual references only.

Otonomy, the Otonomy logo and other trademarks or service marks of Otonomy are the property of Otonomy. Other service marks, trademarks, and tradenames referred to in this Annual Report are the property of their respective owners. Except as set forth above and solely for convenience, the trademarks and tradenames in this Annual Report are referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012. We will remain an "emerging growth company" for up to five years following the completion of our initial public offering, or December 31, 2019, although, if we have more than $1.07 billion in annual revenue, the market value of our common stock that is held by non-affiliates exceeds $700 million as of June 30 of any year, or we issue more than $1.0 billion of non-convertible debt over a three-year period before the end of that five-year period, we would cease to be an "emerging growth company" as of the following December 31. We refer to the Jumpstart Our Business Startups Act of

2012 herein as the “JOBS Act,” and references herein to “emerging growth company” are intended to have the meaning associated with it in the JOBS Act.

ITEM 1A. RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as all other information included in this Annual Report on Form 10-K, including our financial statements, the notes thereto and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations." If any of the following risks actually occurs, our business, financial condition, operating results, prospects and ability to accomplish our strategic objectives could be materially harmed. As a result, the trading price of our common stock could decline and you could lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations and the market price of our common stock.

Risks Related to Our Financial Condition and Capital Requirements

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

We are a commercial-stage biopharmaceutical company with a limited operating history upon which you can evaluate our business and prospects. We are not profitable and have incurred losses in each year since we commenced operations in 2008. In addition, we have limited experience and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical industry. Drug development is a highly speculative undertaking and involves a substantial degree of risk. To date, we have obtained U.S. regulatory approval and launched a single product, OTIPRIO, but have not yet generated significant revenue. We continue to incur significant research and development expenses related to our clinical trials and product development activities and other selling, general and administrative expenses. We have recorded net losses of $90.1 million, $110.6 million and $61.7 million for the years ended December 31, 2017, 2016 and 2015, respectively. As of December 31, 2017, we had an accumulated deficit of $364.9 million.

We have not yet generated significant product revenue and may never become profitable.

We expect to continue to incur significant losses for the foreseeable future. Our ability to achieve significant revenue and profitability is dependent on our ability to complete the development of our product candidates, obtain necessary regulatory approvals and successfully commercialize our products. We may never succeed in these activities and may never generate revenue that is significant or large enough to achieve profitability. We launched OTIPRIO in March 2016, but we have not generated significant revenue from sales of OTIPRIO, and in November 2017, we announced the discontinuation of promotional support for OTIPRIO and are evaluating commercial partnering options for the product, including divestiture. Even if we achieve profitability in the future, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital and any failure to become and remain profitable may adversely affect the market price of our common stock, our ability to raise capital, and our viability.

We may require additional financing to obtain regulatory approval for OTIVIDEX, OTO-313, OTO-413 and any other product candidates, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our commercialization efforts, product development, or other operations.

Since our inception, most of our resources have been dedicated to the development of OTIPRIO and our product candidates, OTIVIDEX and OTO-311 (now OTO-313). In particular, conducting clinical trials for OTIVIDEX, OTO-313 and OTO-413 will require substantial funds. We have funded our operations primarily through the sale and issuance of common stock, convertible preferred stock and convertible notes. As of December 31, 2017, we had cash,

cash equivalents and short-term investments of $120.0 million. We believe that we will continue to expend substantial resources for the foreseeable future for the continued development of OTIVIDEX, OTO-313, OTO-413 and any other product candidates we may choose to pursue. These expenditures will include costs associated with marketing and selling any products approved for sale, manufacturing, preparing regulatory submissions, and conducting nonclinical

studies and clinical trials. We cannot estimate with reasonable certainty the actual amounts necessary to successfully complete the development and commercialization of our product candidates.

Our future capital requirements depend on many factors, including:

- the revenue generated by OTIPRIO and our product candidates, if approved;
- the timing of, and the costs involved in, nonclinical and clinical development and obtaining regulatory approvals for OTIVIDEX, OTO-313, OTO-413 or any other product candidates;
- the cost of manufacturing OTIPRIO and our product candidates;
    - the cost of commercialization activities for our product candidates that may be approved for sale, if any, including marketing, sales and distribution costs;
- the number and characteristics of any other product candidates we develop or acquire;
    - our ability to establish and maintain strategic collaborations, licensing, development, or commercialization arrangements and the terms and timing of such arrangements;
- the degree and rate of market acceptance of OTIPRIO and any other approved products;
- the emergence, approval, availability, perceived advantages, relative cost, relative safety and relative efficacy of other products or treatments;
- the expenses needed to attract and retain skilled personnel;
- the costs associated with being a public company;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims and other intellectual property rights, including litigation costs and the outcome of such litigation;
- the extent to which we are required to pay milestone or other payments under our in-license agreements and the timing of such payments; and
- the cost of litigation, including any product liability or other lawsuits related to our products.

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

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

We may not be able to complete a divestiture or commercial partnership for OTIPRIO.

We have discontinued our promotional support for OTIPRIO and are evaluating commercial partnering options for the product, including divestiture. We cannot predict if any such arrangement would be available at all or whether they would be available on commercially reasonable terms. If we are unable to enter into any such arrangement on acceptable terms or at all, we may not be able to generate much, if any, value from this asset.

Risks Related to Our Product and Product Candidates

We are dependent upon the clinical, regulatory and commercial success of OTIVIDEX for Ménière's disease.

We have invested substantial resources in the development of OTIVIDEX. We have recently completed two Phase 3 trials for OTIVIDEX in Ménière's disease patients. The AVERTS-2 trial, conducted in Europe, achieved its primary endpoint while the AVERTS-1 trial, conducted in the United States, did not. Based on a recent Type C meeting with the FDA, we believe that one additional successful pivotal trial is sufficient to support the U.S. registration of OTIVIDEX in Ménière's disease. We expect to initiate this trial in mid-2018.

OTIVIDEX is most subject to the risks associated with completing future clinical trials, including risks associated with:

- the successful implementation, enrollment and completion of future clinical trials of OTIVIDEX;
- the use and adequacy of patient reported outcomes in future clinical trials;
- our ability to demonstrate with substantial clinical evidence the safety and efficacy of OTIVIDEX in future clinical trials;
- the successful implementation and completion of any additional clinical safety studies or any additional non-clinical studies that may be required by the FDA; and
- the ability to submit an NDA for regulatory approval to the FDA.

If we are able to successfully complete any additional clinical trials required for OTIVIDEX registration, its success will still remain subject to the risks associated with obtaining regulatory approval from the FDA and being manufactured and commercialized, including risks associated with:

- the successful completion of all non-clinical studies required to support regulatory approval by the FDA;
- the timing of review, as the FDA's grant of Fast Track designation for OTIVIDEX does not guarantee priority review;
- the FDA's acceptance of our NDA submission for OTIVIDEX;
- the successful and timely receipt of necessary marketing approval from the FDA to allow us to begin commercializing OTIVIDEX in the United States;
- the ability to manufacture commercial supplies of OTIVIDEX in compliance with cGMP;
- our success in selling OTIVIDEX and achieving broad market acceptance;
- our success in educating physicians and patients about the benefits, administration and use of OTIVIDEX;
- the availability, perceived advantages, relative cost, relative safety and relative efficacy of other products or treatments for Ménière's disease;
- patient demand for the treatment of Ménière's disease;
- the availability of coverage and adequate reimbursement for OTIVIDEX;

- our ability to enforce our intellectual property rights in and to OTIVIDEX; and
- a continued acceptable safety profile of OTIVIDEX following approval.

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

In addition to OTIVIDEX, our long-term prospects depend in part upon advancing additional product candidates, such as OTO-313 and OTO-413, through clinical development to regulatory approval and commercialization.

Although we are focused upon continued development, regulatory approval and commercialization of OTIVIDEX, the development of OTO-313, OTO-413 and other product candidates for the treatment of inner ear disorders is a key element of our long-term strategy. These programs are currently most subject to the risks associated with nonclinical and clinical development, including the risks associated with:

- generating sufficient data to support the initiation or continuation of clinical trials;
- obtaining regulatory approval to commence clinical trials;
- contracting with the necessary parties to conduct clinical trials;
- enrolling sufficient numbers of subjects or patients in clinical trials;
- the timely manufacture of sufficient quantities of the product candidate for use in clinical trials; and
- adverse events in the clinical trials.

Even if we successfully advance OTO-313 through clinical development, or advance OTO-413 or other product candidates from our hearing loss programs or any other future product candidate into clinical development, their success will be subject to all of the clinical, regulatory and commercial risks described elsewhere in this "Risk Factors" section. Accordingly, we cannot assure you that we will ever be able to develop, obtain regulatory approval of, commercialize or generate significant revenue from OTO-313, OTO-413, any other product candidate from our hearing loss programs or any other future product candidate.

Risks Related to Our Business and Strategy

OTIPRIO and our product candidates, OTIVIDEX, OTO-313, OTO-413 or any future product candidates that obtain regulatory approval, may fail to achieve the broad degree of market acceptance and use necessary for commercial success.

OTIPRIO and our product candidates, if approved, may not achieve market acceptance among physicians and patients, and may not be commercially successful. For OTIPRIO, treatment of pediatric patients with bilateral otitis media with effusion undergoing TTP surgery is currently addressed with the off-label use of antibiotic ear drops, but antibiotic ear drops are approved for the AOE indication. We launched OTIPRIO in March 2016, but we have not generated significant revenue from sales of OTIPRIO, and in November 2017, we announced the discontinuation of promotional support for OTIPRIO and are evaluating commercial partnering options for the product, including divestiture.

There are currently no FDA-approved drug treatments for the indications we are pursuing for our product candidates. Our proposed initial indication for OTIVIDEX is the treatment of vertigo associated with Ménière's disease. Currently, Ménière's disease patients are routinely prescribed a low-salt diet and off-label use of diuretics. Physicians may also prescribe the off-label use of antihistamines, anticholinergics, phenothiazines and benzodiazepines as well as corticosteroids. Our proposed indication for OTO-313 is the treatment of tinnitus. Currently, physicians may attempt to treat tinnitus symptoms with the off-label use of steroids, anxiolytics, antidepressants, and antipsychotics. Our target indication for OTO-413 is the treatment of speech-in-noise hearing

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difficulties. A subset of patients with this condition are currently treated with hearing aids. The commercial success of OTIPRIO and our product candidates, if approved, will depend significantly on the adoption and use of the resulting product by physicians for approved indications. The decision to elect treatment with OTIPRIO for middle ear effusion in pediatric patients requiring TTP surgery and AOE, or to elect to utilize OTIVIDEX for Ménière's disease, or OTO-313 for tinnitus, or OTO-413 for speech-in-noise hearing difficulties, rather than other products or treatments, may be influenced by a number of factors, including:

- the cost, safety and effectiveness of our products as compared to other products or treatments;
- physician willingness to adopt our product in lieu of other products or treatments;
- ability to gain utilization in facilities responsible for purchasing our products;
- the extent to which physicians recommend our products to their patients;
- patient or caregiver sentiment about the benefits and risks of our products;
- proper training and administration of our products by physicians and medical staff, such that their patients do not experience excessive discomfort during treatment or adverse side effects;
- the procedural risks of IT injection;
- overcoming any biases physicians or patients may have in favor of other products or treatments;
- patient preference for non-injectable treatments;
- patient or caregiver satisfaction with the results and administration of our product and overall treatment experience, including relative convenience and ease of administration;
- the effectiveness of our sales and marketing efforts;
- demand for the treatment of the relevant diseases or disorders;
- product labeling or product insert requirements of the FDA or other regulatory authorities;
- the prevalence and severity of any adverse events;
- the revenue and profitability that our products will offer a physician as compared to other products or treatments;
- the availability of coverage and adequate reimbursement by third-party payors and government authorities and perceptions regarding such availability; and
- general patient or caregiver confidence, which may be impacted by economic and political conditions.

If our product candidates, if approved for use, fail to achieve the broad degree of market acceptance necessary for commercial success, our operating results and financial condition will be adversely affected. In addition, even if any of our products gain acceptance, the markets for treatment of patients with our target indications may not be as significant as we estimate.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, results of earlier studies and trials may not be predictive of future trial results, and our clinical trials may fail to adequately demonstrate the safety and efficacy of our product candidates.

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

clinical trials are completed, the results may not be sufficient to obtain regulatory approval for our product candidates or support the indications which we are pursuing.

We have in the past experienced delays in our clinical trials and we may in the future. We do not know whether future clinical trials, if any, will begin on time, need to be redesigned, enroll an adequate number of patients on time or be completed on schedule, if at all. Clinical trials can be delayed, suspended or terminated for a variety of reasons, including failure to:

- generate sufficient nonclinical, toxicology, or other in vivo or in vitro data to support the initiation or continuation of clinical trials;
- obtain regulatory approval, or feedback on trial design, to commence a clinical trial;
- identify, recruit and train suitable clinical investigators;
- reach agreement on acceptable terms with prospective CROs, and clinical trial sites;
- obtain and maintain institutional review board (IRB) approval at each clinical trial site;
- identify, recruit and enroll suitable patients to participate in a clinical trial;
- have a sufficient number of patients complete a clinical trial or return for post-treatment follow-up;
- ensure clinical investigators observe trial protocol and comply with Good Clinical Practices (GCP) or continue to participate in a clinical trial;
- address any patient safety concerns that arise during the course of a clinical trial;
- address any conflicts with new or existing laws or regulations;
- add a sufficient number of clinical trial sites;
- timely manufacture sufficient quantities of product candidate for use in clinical trials; or
- have sufficient capital to fund a clinical trial.

Patient enrollment is a significant factor in the timing of clinical trials. We may not be able to initiate or continue clinical trials for our product candidates on a timely basis if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials. Patient enrollment is affected by many factors, including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the clinical trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' or caregivers' perceptions as to the potential advantages of the drug candidate being studied in relation to other available therapies, including any new drugs or treatments that may be approved for the indications we are investigating.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the data safety monitoring board for such clinical trial or by the FDA or any other regulatory authority, or if the IRBs of the institutions in which such clinical trials are being conducted suspend or terminate the participation of their clinical investigators and sites subject to their review. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

For example, OTIVIDEX was previously subject to Full Clinical Hold that was removed in July 2013 and then subject to Partial Clinical Hold that was removed in June 2014. The removal of Full Clinical Hold allowed us to initiate the Phase 2b clinical trial. As a result of OTIVIDEX being placed on Full Clinical Hold, OTIPRIO was also placed on Full Clinical Hold. The OTIPRIO Full Clinical Hold was removed in November 2012. We cannot assure you that our product candidates will not be subject to new clinical holds or significant delay in the future.

If we experience delays in the initiation or completion of any clinical trial of our product candidates for any reason, or if any clinical trial is terminated, the commercial prospects of our product candidates may be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may significantly harm our business, financial condition and prospects. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

We may be unable to obtain regulatory approval for our product candidates other than OTIPRIO. The denial or delay of any such approval would delay commercialization and have a material adverse effect on our potential to generate revenue, our business and our results of operations.

The research, development, testing, manufacturing, labeling, packaging, approval, promotion, advertising, storage, recordkeeping, marketing, distribution, post-approval monitoring and reporting, and export and import of drug products are subject to extensive regulation by the FDA and by foreign regulatory authorities in other countries. These regulations differ from country to country. To gain approval to market our product candidates, we must provide clinical data that demonstrates with substantial evidence the safety and efficacy of the product for the intended indication. Other than OTIPRIO in the United States, we have not yet obtained regulatory approval to market any of our other product candidates in the United States or any other country. Our business depends upon obtaining these regulatory approvals.

The FDA can delay, limit or deny approval of our product candidates for many reasons, including:

- our inability to satisfactorily demonstrate that the product candidates are safe and effective for the requested indication;
- the FDA's disagreement with our trial protocol or the interpretation of data from nonclinical studies or clinical trials;
- the population studied in the clinical trial may not be sufficiently broad or representative to assess safety in the full population for which we seek approval;
- our inability to demonstrate that clinical or other benefits of our product candidates outweigh any safety or other perceived risks;
- the FDA's determination that additional nonclinical or clinical trials are required;
    - the FDA's non-approval of the formulation, labeling or the specifications of our product candidates;
- the FDA's failure to accept the manufacturing processes or facilities of third-party manufacturers with which we contract, or our inability to manufacture our product candidates pursuant to cGMP; or
- the potential for approval policies or regulations of the FDA to significantly change in a manner rendering our clinical data insufficient for approval.

Even if we eventually complete clinical testing and receive approval of any regulatory filing for our product candidates, the FDA may grant approval contingent on the performance of costly additional post-approval clinical trials. The FDA may also approve our product candidates for a more limited indication or a narrower patient population than we originally requested, and the FDA may not approve the labeling that we believe is necessary or desirable for the successful commercialization of our product candidates. To the extent we seek regulatory approval in foreign countries, we may face challenges similar to those described above with regulatory authorities in applicable jurisdictions. Any delay in obtaining, or inability to obtain, applicable regulatory approval for any of our product candidates would delay or prevent commercialization of our product candidates and would materially adversely impact our business, results of operations and prospects.

Use of our product or product candidates could be associated with undesirable side effects or adverse events that could halt their clinical development, delay or prevent their regulatory approval, limit their commercial potential or result in significant negative consequences.

Our product or product candidates could be associated with side effects or adverse events which can vary in severity and frequency. Side effects or adverse events associated with the use of our product or product candidates may be observed at any time, including in clinical trials or once a product is commercialized, and any such side effects or adverse events may negatively affect our ability to obtain regulatory approval for our product candidates or market our product or product candidates, if approved. Side effects such as toxicity or other safety issues associated with the use of our product or product candidates could require us to perform additional studies or halt development or sale of our product or product candidates or expose us to product liability lawsuits which will harm our business. We may be required by regulatory agencies to conduct additional nonclinical or clinical trials regarding the safety and efficacy of our product or product candidates which we have not planned or anticipated. We cannot assure you that we will resolve any issues related to any product-related adverse events to the satisfaction of the FDA or any regulatory agency in a timely manner or ever, which could harm our business, prospects and financial condition.

Some patients in our clinical trials have reported adverse events after being treated with OTIPRIO and OTIVIDEX. If we are successful in commercializing our product or product candidates, the FDA and other foreign regulatory agency regulations will require that we promptly report certain information about adverse medical events if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We may fail to report adverse events we become aware of within the prescribed timeframe. We may also fail to appreciate that we have become aware of a reportable adverse event, especially if it is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of our product or product candidates. If we fail to comply with our reporting obligations, the FDA or other foreign regulatory agencies could take action including criminal prosecution, the imposition of civil monetary penalties, seizure of our products, or delay in approval or clearance of future products.

OTIPRIO and our product candidates, if approved, will face significant competition in the biopharmaceutical industry, and our failure to effectively compete with competitor drugs, including off-label drug use, and future competitors may prevent us from achieving significant market penetration and expansion.

The biopharmaceutical industry is intensely competitive and subject to rapid and significant technological change. If approved, our products must compete with off-label drug use by physicians to treat the indications for which we seek approval, such as, in the case of OTIPRIO, the current use of inexpensive generic antibiotic ear drops to treat middle ear effusion in patients requiring TTP surgery. We are also aware that other companies, such as Arbor Pharmaceuticals, LLC, Auris Medical Holding AG, Autifony Therapeutics Ltd., Fennec Pharmaceuticals Inc., Frequency Therapeutics, KYORIN Pharmaceutical Co. Ltd., Laboratorios SALVAT S.A., Metarmor Inc., Novartis AG, Novus Therapeutics, Inc. (formerly Otic Pharma Ltd.), Oricula Therapeutics LLC, Otologic Pharmaceutics Inc., Sensorion SA, Sound Pharmaceuticals Inc., Strekin AG and Synphora AB, are commercializing products or conducting clinical trials for potential products for the treatment of various otic indications, including ear infections, tinnitus, Ménière's disease and hearing loss. Many companies in the biopharmaceutical industry have greater resources to discover, obtain patents, develop, test and obtain regulatory approvals for products, as well as commercialize, market and promote approved products, including communicating the effectiveness, safety and value of products to actual and prospective customers and medical staff. These companies may develop new drugs to treat the diseases and disorders we target, or seek to have existing drugs approved for use for new indications that treat the diseases and disorders we target. Mergers and acquisitions in the biopharmaceutical industry may result in even more resources being concentrated in potential competitors. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in this industry. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis products that are more effective, easier to administer or less costly than our product or product candidates.

We rely on third parties to conduct many of our nonclinical studies and all of our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be unable to obtain regulatory approval for, or commercialize, our product candidates.

We do not have the ability to independently conduct many of our nonclinical studies or any of our clinical trials. We rely on medical institutions, clinical investigators, contract laboratories, and other third parties, such as CROs, to conduct clinical trials on our product candidates. Third parties play a significant role in the conduct of our clinical trials and the subsequent collection and analysis of data. These third parties are not our employees, and except for remedies available to us under our agreements, we have limited ability to control the amount or timing of resources that any such third party will devote to our clinical trials. If our CROs or any other third parties upon which we rely for administration and conduct of our clinical trials do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements, or for other reasons, or if they otherwise perform in a substandard manner, our clinical trials may be extended, delayed, suspended or terminated, and we may not be able to complete development of, obtain regulatory approval for, or successfully commercialize our product candidates.

We and the third parties upon whom we rely are required to comply with GCP, which are regulations and guidelines enforced by regulatory authorities around the world for products in clinical development. Regulatory authorities enforce these GCP regulations through periodic inspections of clinical trial sponsors, principal investigators and clinical trial sites. If we or our third parties fail to comply with applicable GCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and our submission of marketing applications may be delayed or the regulatory authorities may require us to perform additional clinical trials before reviewing or approving our marketing applications. We cannot assure you that, upon inspection, a regulatory authority will determine that any of our clinical trials comply or complied with applicable GCP regulations.

In addition, our clinical trials must be conducted with drug supply produced under cGMP regulations, which are enforced by regulatory authorities. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be impacted if our CROs, clinical investigators or other third parties violate federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws. In order for our clinical trials to be carried out effectively and

efficiently, it is imperative that our CROs and other third parties communicate and coordinate with one another. Moreover, our CROs and other third parties may also have relationships with other commercial entities, some of which may compete with us. Our CROs and other third parties may terminate their agreements with us upon as few as 30 days' notice under certain circumstances. If our CROs or other third parties conducting our clinical trials do not perform their contractual duties or obligations, experience work stoppages, do not meet expected deadlines, terminate their agreements with us or need to be replaced, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical trial protocols or GCPs, or for any other reason, we may need to conduct additional clinical trials or enter into new arrangements with alternative CROs, clinical investigators or other third parties. We may be unable to enter into arrangements with alternative CROs, clinical investigators or other third parties on commercially reasonable terms, or at all. Switching or adding CROs, clinical investigators or other third parties can involve substantial cost and require extensive management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. Although we carefully manage our relationship with our CROs, clinical investigators and other third parties, there can be no assurance that we will not encounter such challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, prospects, financial condition or results of operations

We rely completely on third parties to manufacture our nonclinical, clinical drug supplies and commercial supplies of OTIPRIO and any other approved products.

We outsource the manufacture of OTIPRIO and our product candidates. We do not currently have the infrastructure or internal capability to manufacture supplies of OTIPRIO or our product candidates for use in development and commercialization. If we were to experience an unexpected loss of supply of OTIPRIO or our product candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, our business would be harmed, and we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing clinical trials. Although we generally do not begin a clinical trial unless we believe we have a sufficient supply of a product candidate to complete the clinical trial, we may be required to manufacture additional supplies of our product candidates to the extent our estimates of the amounts required prove inaccurate, we suffer unexpected losses of product candidate supplies, or to the extent that we are required to have fresh product candidate supplies manufactured to satisfy regulatory requirements or specifications. Any significant delay or discontinuation in the supply of OTIPRIO or a product candidate, or the raw material components thereof, due to the need to replace a contract manufacturer or other third-party manufacturer, could considerably harm our business and ability to generate revenue and delay completion of our clinical trials, product testing and potential regulatory approval of our product candidates.

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, and the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us. The facilities used by our third-party manufacturers must be accepted by the FDA pursuant to inspections that will be conducted before approval and after we submit our NDA to the FDA. We do not control the implementation of the manufacturing process of, and are completely dependent on, our third-party manufacturers for compliance with the regulatory requirements, for manufacture of both active drug substances and finished drug products. If our third-party manufacturers cannot successfully manufacture material that conforms to applicable specifications in our regulatory applications and the strict regulatory requirements of the FDA or foreign regulatory authorities, we will not be able to secure and/or maintain regulatory acceptance of our contract manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers or other third-party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. The failure of our third-party manufacturers to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and

criminal prosecutions, any of which could significantly and adversely affect supplies of OTIPRIO or our product candidates or any other product candidates or products that we may develop. In addition, if the FDA does not accept these facilities for the manufacture of our product or our product candidates or if it withdraws any such acceptance in the future, we will need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Any failure or refusal to supply the components for our product or our product candidates could delay, prevent or impair our clinical development or commercialization efforts. If our contract manufacturers were to breach or terminate their manufacturing arrangements with us, the development or

commercialization of the affected product or product candidates could be delayed, which could have an adverse effect on our business. Any change in our manufacturers could be costly because the commercial terms of any new arrangement could be less favorable and because the expenses relating to the transfer of necessary technology and processes could be significant.

We may encounter issues with manufacturing as we commercialize OTIPRIO or our product candidates, if approved.

We have limited experience manufacturing OTIPRIO for commercial use, and our product candidates have never been manufactured for commercial use. There are risks associated with manufacturing for commercial use including, among others, potential problems with forecasting and cost overruns, process reproducibility, storage availability, stability issues, lot consistency and timely availability of materials. We cannot assure you that our contract manufacturers will be able to manufacture any approved product to specifications acceptable to the FDA or foreign regulatory authorities, or to produce it in sufficient quantities to meet the market demand. We have in the past manufactured, and may in the future manufacture, batches of OTIPRIO that do not meet the appropriate specifications and cannot be used. We may also manufacture OTIPRIO or any approved product that remains unused due to obsolescence, expiry or quantities in excess of expected demand. If our contract manufacturers are unable to successfully produce sufficient quantities of any approved product for commercialization, our commercial efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

We depend on a small number of suppliers for the raw materials necessary to produce OTIPRIO and our product candidates. The loss of these suppliers, or their failure to supply us with these raw materials, would materially and adversely affect our business.

We depend on the availability of key raw materials, including poloxamer for OTIPRIO and our product candidates, ciprofloxacin for OTIPRIO, dexamethasone for OTIVIDEX, gacyclidine for OTO-313 and BDNF for OTO-413, from a small number of third-party suppliers. Because there are a limited number of suppliers for the raw materials that we use to manufacture our product and product candidates, we may need to engage alternate suppliers to prevent a possible disruption of the manufacture of the materials necessary to produce OTIPRIO for required commercial supplies or our product candidates for our clinical trials. We do not have any control over the availability of raw materials. If we or our manufacturers are unable to purchase these raw materials on acceptable terms, at sufficient quality levels, or in adequate quantities, if at all, commercial sales of OTIPRIO and the development of OTIVIDEX, OTO-313, OTO-413 or any future product candidates, would be delayed or there would be a shortage in supply, which would impair our ability to meet our development objectives for our product candidates or generate revenues from the sale of any approved products.

Our ability to market OTIPRIO is limited to its approved indications, and our product candidates, if approved, will be limited to certain indications. If we want to expand the indications for which we may market our products, we will need to obtain additional regulatory approvals, which may not be granted.

OTIPRIO is currently approved for the treatment of pediatric patients with bilateral otitis media with effusion undergoing TTP surgery and for the treatment of AOE and is in development for AOMT. We are developing OTIVIDEX for the treatment of vertigo associated with Ménière’s disease, OTO-313 for the treatment of tinnitus and OTO-413 for the treatment of speech-in-noise hearing difficulties. The FDA and other applicable regulatory agencies will restrict our ability to market and advertise our products to the scope of the approved label for the applicable product and for no other indications, which could limit physician and patient adoption. We may attempt to develop new treatment indications for our product or product candidates in the future, but we cannot predict when or if we will receive the regulatory approvals required to promote our product or product candidates for new treatment indications. Failure to receive such approvals prevents us from promoting and commercializing the new treatment indications. In

addition, we would be required to conduct additional clinical trials or studies to support approvals for additional indications, which would be time consuming and expensive, and may produce results that do not support regulatory approvals. If we do not obtain additional regulatory approvals, our ability to expand our business will be limited.

If our product candidates are approved for marketing, and we are found to have improperly promoted off-label uses, or if physicians misuse our products, we may become subject to prohibitions on the sale or marketing of our products, significant sanctions and product liability claims, and our image and reputation within the industry and marketplace could be harmed.

The FDA and other regulatory agencies strictly regulate the marketing and promotional claims that are made about drug products. In particular, a product may not be promoted for uses or indications that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. For example, OTIPRIO is approved for the treatment of pediatric patients with bilateral otitis media with effusion undergoing TTP surgery and for the treatment of AOE, and we cannot promote the use of our product in a manner that is inconsistent with the approved label. Although physicians are able to, in their independent medical judgment, use OTIPRIO on their patients in an off-label manner, such as for the treatment of other otic indications, if we are found to have promoted such off-label uses, we may receive warning letters and become subject to significant liability, which would materially harm our business. The federal government has levied large administrative, civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. If we become the target of such an investigation or prosecution based on our marketing and promotional practices, we could face similar sanctions, which would materially harm our business. In addition, management's attention could be diverted from our business operations, significant legal expenses could be incurred, and our reputation could be damaged. The federal government and regulatory authorities have also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we are deemed by the federal government or regulatory authorities to have engaged in the promotion of our products for off-label use, we could be subject to prohibitions on the sale or marketing of our products or significant fines and penalties, and the imposition of these sanctions could also affect our reputation with physicians, patients and caregivers, and our position within the industry.

Physicians may also misuse our products or use improper techniques, potentially leading to adverse results, side effects or injury, which may lead to product liability claims and costly litigation. Product liability claims could divert management's attention from our core business, be expensive to defend, and result in sizable damage awards against us that may not be covered by insurance. We currently carry product liability insurance with policy limits that we believe are customary for similarly situated companies and adequate to provide us with coverage for foreseeable risks. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Furthermore, the use of our products for conditions other than those approved by the FDA may not effectively treat such conditions, which could harm our reputation in the marketplace among physicians and patients.

We have limited sales and marketing experience and may be unable to successfully commercialize our products or generate product revenue.

We have limited experience in the marketing and sale of pharmaceutical products, and there are significant risks involved in managing a sales and marketing organization, including our ability to hire, retain, adequately compensate and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel and effectively manage a geographically dispersed sales and marketing team. For example, we recently discontinued promotional support for OTIPRIO and, as a result, no longer have a sales force. If we decide not to promote our product candidates, if approved, ourselves, we may consider promotional partnership arrangements. For instance, we are exploring commercial partnering options for OTIPRIO, including divestiture. If we are unable to enter into such arrangements on acceptable terms or at all, we may not be able to successfully commercialize our products. Any failure or delay in entering promotional partnerships or developing our internal sales, marketing and distribution capabilities would adversely impact the commercialization of our products. If we are not successful in

commercializing our products, either on our own or through partnering with one or more third parties, our future product revenue will suffer and we would incur significant additional losses.

To expand our development and commercial support capabilities in the future, we may need to increase the size of our organization, and we may experience difficulties in managing this growth.

As we advance our product candidates through the development process and commercialize our product candidates, if approved, we may need to expand our development, regulatory, quality, managerial, sales and

marketing, operational, finance and other resources to manage our operations and clinical trials, continue our development activities and commercialize our product candidates, if approved. If our operations expand, we expect that we will need to manage additional relationships with various manufacturers and collaborative partners, suppliers and other organizations.

Due to our limited financial resources and our limited experience in managing a company with such growth, we may not be able to effectively manage the expansion of our operations or recruit, train and retain additional qualified personnel. For example, in December 2016, we moved into our new headquarters location in San Diego, California. The physical expansion of our operations has led to significant costs. Any inability to manage growth could delay the execution of our development and strategic objectives, or disrupt our operations, which could materially impact our business, revenue and operating results.

Coverage and reimbursement decisions by third-party payors may have an adverse effect on pricing and market acceptance. Recent legislative and regulatory activity may exert downward pressure on potential pricing and reimbursement for our products, if approved, that could materially affect the opportunity to commercialize.

There is significant uncertainty related to the third-party coverage and reimbursement of newly approved drugs. Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Therefore, market acceptance and sales of our products, if approved, in both domestic and international markets will depend significantly on the availability of adequate coverage and reimbursement from third-party or government payors for any of our products and may be affected by existing and future healthcare reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will cover and establish payment levels. CMS has established a unique J Code for OTIPRIO that replaces a previously assigned C Code. We also intend to apply for a unique J Code for OTIVIDEX, OTO-313 and OTO-413. We cannot assure you that J Codes will be issued for OTIVIDEX, OTO-313 and OTO-413, if approved. We also cannot assure you that third-party payors will provide reimbursement according to a J Code. If a J Code is not issued or a J Code is issued but not reimbursed by third-party payors, then the cost of these drugs may be absorbed by healthcare providers or charged to patients. If this is the case, our expectations of the pricing we expect to achieve for OTIPRIO, and OTIVIDEX, OTO-313 and OTO-413, if approved, and the related potential revenue, may be significantly diminished. We cannot be certain that coverage and adequate reimbursement will be available for OTIPRIO or any other products, if approved, or that such coverage and reimbursement will be authorized in a timely fashion, even if a unique J Code is assigned for such products. Also, we cannot be certain that reimbursement policies will not reduce the demand for, or the price paid for, OTIPRIO or any of our product candidates, if approved. If reimbursement is not available or is available on a limited basis for any of our products, if approved, we may not be able to successfully commercialize any such products. Reimbursement by a third-party or government payor may depend upon a number of factors, including, without limitation, the third-party or government payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Obtaining coverage and reimbursement approval for a product from a government or other third-party payor is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to the payor. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement or to have pricing set at a satisfactory level. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels such as may result where alternative or generic treatments are available, we may be unable to achieve or sustain profitability.

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Assuming we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate or may require co-payments that patients find unacceptably high. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products.

In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained. In some foreign countries, particularly in Europe, 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 additional clinical trials that compare the cost-effectiveness of our products to other available therapies. If reimbursement of any of our products, if approved, is unavailable or limited in scope or amount in a particular country, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability of our products in such country.

The United States and several other jurisdictions are considering, or have already enacted, a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell any of our products profitably, if approved. Among policy-makers and payors in the United States and elsewhere, there has been significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access to healthcare. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. There have been, and likely will continue to be, legislative and regulatory proposals at the federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. We cannot predict if or how these or future initiatives may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the demand for any of our products, if approved;
- the ability to set a price that we believe is fair for any of our products, if approved;
- our ability to generate revenues and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

In March 2010, the ACA became law in the United States. One goal of ACA is to reduce the cost of healthcare and substantially change the way healthcare is financed by both governmental and private insurers. While we cannot fully predict what impact on federal reimbursement policies this legislation will have in general or on our business specifically, ACA may result in downward pressure on pharmaceutical reimbursement, which could negatively affect our ability to generate revenue, achieve market acceptance of our product or future approved products, attain profitability, or commercialize our product or any future approved products. Provisions of ACA relevant to the pharmaceutical industry include the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, not including orphan drug sales;
- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts on negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer’s outpatient drugs to be covered under Medicare Part D;

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- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report annually certain financial arrangements with physicians and teaching hospitals, as defined in ACA and its implementing regulations, including reporting any payment or "transfer of value" provided to physicians and teaching hospitals and any ownership and investment interests held by physicians and their immediate family members during the preceding calendar year;
- expansion of healthcare fraud and abuse laws, including the federal False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research.

Recent changes in the U.S. government could lead to repeal of or changes in some or all of the ACA, and complying with any new legislation or reversing changes implemented under the ACA could be time-intensive and expensive, resulting in a material adverse effect on our business. Healthcare reform measures that may be adopted in the future may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for our product or future approved products. Any such reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, achieve market acceptance of our product or future approved products, attain profitability, or commercialize future approved products. Until the ACA or other healthcare reform measures are fully implemented or there is more certainty concerning the future of the ACA or such healthcare reform measures, it will be difficult to predict its full impact and influence on our business.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our products.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and face an even greater risk now that OTIPRIO has been commercialized and as other product candidates get approved, if at all. For example, we may be sued if any product we develop allegedly causes or is perceived to cause injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our products. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our products;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants or cancellation of clinical trials;
- costs to defend the related litigation;
- a diversion of management's time and our resources;

- substantial monetary awards to clinical trial participants or patients;
- regulatory investigations, product recalls, withdrawals or labeling, marketing or promotional restrictions;
- exhaustion of any available insurance and our capital resources;
- loss of revenue; and
- the inability to commercialize any products we develop.

Our inability to obtain and maintain sufficient product liability insurance at an acceptable cost and scope of coverage to protect against potential product liability claims could prevent or inhibit the commercialization of our products. We currently carry product liability insurance with policy limits that we believe are customary for similarly situated companies and adequate to provide us with coverage for foreseeable risks. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. If we determine that it is prudent to increase our product liability coverage in the future, we may be unable to obtain such increased coverage on acceptable terms, or at all. Our insurance policies also have various exclusions and deductibles, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses.

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

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management, commercial, clinical and scientific personnel. We believe that our future success is highly dependent upon the contributions of our senior management, particularly our President and Chief Executive Officer, as well as our senior scientists and other members of our senior management team. The loss of services of any of these individuals, who all have at-will employment arrangements with us, could delay or prevent the successful development of our product pipeline, completion of our planned clinical trials or the commercialization of our product candidates, if approved.

Although we have not historically experienced unique difficulties attracting and retaining qualified employees, we could experience such problems in the future. For example, competition for qualified personnel in the biotechnology and pharmaceuticals field is intense due to the limited number of individuals who possess the skills and experience required by our industry. We will need to hire additional personnel as we expand our clinical development and commercial activities. We may not be able to attract and retain quality personnel on acceptable terms, or at all, which may cause our business and operating results to suffer.

If we are not successful in discovering, developing, acquiring and commercializing additional product candidates, our ability to expand our business and achieve our strategic objectives would be impaired.

Although a substantial amount of our efforts are focused on the development and regulatory approval of our current product candidates, a key element of our strategy is to identify, develop and commercialize additional product candidates for the treatment of inner ear disorders. We are seeking to do so through our internal research programs and may explore strategic collaborations with third parties for the development or acquisition of new product candidates or products. Research programs to identify new product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified or successfully developed.

Our internal computer systems, or those of our CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our drug development programs.

We rely on information technology systems to keep financial records, maintain laboratory and corporate records, communicate with staff and external parties and operate other critical functions. Despite the implementation of security measures, our internal computer systems and those of our third-party logistics vendor, CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. To our knowledge, we have not experienced a material system failure, accident or security breach to date, and if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our commercialization activities or drug development programs. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the development and commercialization of our product candidates could be delayed.

Changes in financial accounting standards or practices may cause adverse, unexpected financial reporting fluctuations and affect our reported operating results.

Generally accepted accounting principles in the United States are subject to interpretation by the FASB, the SEC and various bodies formed to promulgate and interpret appropriate accounting principles. A change in accounting standards or practices can have a significant effect on our reported results and may even affect our reporting of transactions completed before the change is effective. New accounting pronouncements and varying interpretations of accounting pronouncements have occurred and may occur in the future. Changes to existing rules or the questioning of current practices may adversely affect our reported financial results or the way we conduct our business.

Our employees, independent contractors, clinical investigators, CROs, consultants and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk that our employees, independent contractors, clinical investigators, CROs, consultants and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates: (i) FDA regulations, including those laws requiring the reporting of true, complete and accurate information to the FDA, (ii) manufacturing standards, (iii) federal, state and foreign healthcare fraud and abuse laws, or (iv) laws that require the reporting of financial information or data accurately. Specifically, research, sales, marketing, education and other business arrangements in the healthcare industry are subject to extensive laws intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws may restrict or prohibit a wide range of pricing, discounting, education, marketing and promotion, sales commission, customer incentive programs and other business

arrangements. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of business conduct and ethics, as well as various compliance policies and procedures, but it is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or

unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws. If any such actions are instituted against us, even if we are successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business. Violations of such laws subject us to numerous penalties, including, but not limited to, the imposition of civil, criminal and administrative penalties, damages, monetary fines, disgorgement, individual imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

We or the third parties upon whom we depend may be adversely affected by earthquakes, wildfires or other natural disasters, and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our corporate headquarters are located in the San Diego, which in the past has experienced severe earthquakes. We do not carry earthquake insurance. The San Diego area has also experienced serious wildfires. If a natural disaster or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as product development and research efforts for our current product candidates and finance records, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and may not be adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

Furthermore, integral parties in our supply chain and distribution chain are geographically concentrated and operating from single sites, increasing their vulnerability to natural disasters or other sudden, unforeseen and severe adverse events. If such an event were to affect our supply chain, it could have a material adverse effect on our business.

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 may cause extreme volatility and disruptions in the capital and credit markets and could result in a variety of risks to our business and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers and third-party payors to delay making payments for our services.

Recent events, including the United Kingdom’s 2016 vote in favor of exiting the European Union, or “Brexit,” and the initiation for the United Kingdom’s withdrawal, and similar geopolitical developments or the perception that any of them could occur, may lead to worldwide economic and legal uncertainty, including significant volatility in global stock markets and currency exchange rates, and increasingly divergent laws and regulations.

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 Intellectual Property

If our efforts to protect the intellectual property related to our product and product candidates are not adequate, we may not be able to compete effectively in our market.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our product, product candidates and technology. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, eroding our competitive position in the market.

The patent application process, also known as patent prosecution, is expensive and time-consuming, and we and our current or future licensors and licensees may not be able to prepare, file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we or our current licensors, or any future licensors or licensees, will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, it is possible that certain patentable aspects of our inventions may not be protected in a manner consistent with the best interests of our business. Defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, etc., although we are unaware of any such defects that we believe are of material import. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid and unenforceable. If we or our current licensors, or any future licensors or licensees, fail to file patent applications, or maintain, enforce or protect our patents, such patent rights may be reduced or eliminated. If our current licensors, or any future licensors or licensees, are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

The strength of patents in the pharmaceutical field involves complex legal and scientific questions and can be uncertain. This uncertainty includes changes to the patent laws through either legislative action to change statutory patent law or court action that may reinterpret existing law or rules in ways affecting the scope or validity of issued patents. The patent applications that we own or in-license may fail to result in issued patents in the United States or foreign countries with claims that cover our product or product candidates. Even if patents do successfully issue from the patent applications that we own or in-license, third parties may challenge the validity, enforceability or scope of such patents, which may result in such patents being narrowed, invalidated or held unenforceable. For example, patents granted by the European Patent Office may be challenged, also known as opposed, by any person within nine months from the publication of their grant. Any successful challenge to our patents could deprive us of exclusive rights necessary for the successful commercialization of our product or product candidates. Furthermore, even if they are unchallenged, our patents may not adequately protect our product or product candidates, provide exclusivity for our product or product candidates, or prevent others from designing around our patents. If the breadth or strength of protection provided by the patents we hold or pursue with respect to our product or product candidates is challenged, it could dissuade companies from collaborating with us to develop, or threaten our ability to commercialize our product or product candidates.

Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after its effective filing date. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Without patent protection for our product or product candidates, we may be open to competition from generic versions of our product or product candidates. Further, if we encounter delays in our development efforts, including our clinical trials, the period of time during which we could market our product or product candidates under patent protection would be reduced.

Most of our patents and patent applications are entitled to effective filing dates prior to March 16, 2013. For U.S. patent applications for which patent claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third party, for example a competitor, or instituted by the U.S. Patent and Trademark Office (USPTO) to determine who was the first to invent any of the subject matter covered by those patent claims. An unfavorable outcome could require us either to cease using the related technology or to attempt to license rights from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our participation in an interference proceeding may fail and, even if successful, may result in substantial costs and distract our management.

In addition to the protection afforded by patents, we also rely on trade secret protection to protect proprietary know-how that may not be patentable or that we elect not to patent, processes for which patents may be difficult to obtain or enforce, and any other elements of our product and product candidates, and our product development processes (such as manufacturing and formulation technologies) that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect. If the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating any trade secrets. Misappropriation or unauthorized disclosure of our trade secrets could significantly affect our competitive position and may have a material adverse effect on our business. Furthermore,

trade secret protection does not prevent competitors from independently developing substantially equivalent information and techniques, and we cannot guarantee that our competitors will not independently develop substantially equivalent information and techniques. The FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all.

In an effort to protect our trade secrets and other confidential information, we require our employees, consultants, advisors, and any other third parties that have access to our proprietary know-how, information or technology, for example, third parties involved in the formulation and manufacture of our product and product candidates, and third parties involved in our clinical trials, to execute confidentiality agreements upon the commencement of their relationships with us. These agreements require that all confidential information developed by such employees, consultants, advisors, etc., or made known to them by us during the course of our relationship with them be kept confidential and not disclosed to third parties. However, we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed despite having such confidentiality agreements. Adequate remedies may not exist in the event of unauthorized use or disclosure of our trade secrets. In addition, in some situations, these confidentiality agreements may conflict with, or be subject to, the rights of third parties with whom our employees, consultants, or advisors have previous employment or consulting relationships. To the extent that our employees, consultants or advisors use any intellectual property owned by third parties in their work for us, disputes may arise as to the rights in any related or resulting know-how and inventions. If we are unable to prevent unauthorized material disclosure of our trade secrets to third parties, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results and financial condition.

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

As is the case with other pharmaceutical companies, our success is heavily dependent on intellectual property, particularly on obtaining and enforcing patents. Obtaining and enforcing patents in the pharmaceutical industry involves both technological and legal complexity, and therefore is costly, time-consuming and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation. Further, recent U.S. Supreme Court rulings have either narrowed the scope of patent protection available in certain circumstances or weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained.

For our U.S. patent and patent applications containing a claim not entitled to priority before March 16, 2013, there is a greater level of uncertainty in the patent law. In September 2011, the Leahy-Smith America Invents Act, or the American Invents Act (AIA), was signed into law. The AIA includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. It is not clear what other, if any, impact the AIA will have on the operation of our business. Moreover, the AIA 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.

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a "first-to-file" system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the USPTO after March 16, 2013 but before us could therefore be awarded a patent covering an invention of ours even if we had made

the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Furthermore, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our technology and the prior art allow our technology to be patentable over the prior art. Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to either (i) file any patent application related to our product or product candidates or (ii) invent any of the inventions claimed in our patents or patent applications.

Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and provided opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal court necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party in a district court action.

Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and any patents that we might obtain in the future.

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

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent prosecution process. Periodic maintenance fees and various other governmental fees on any issued patent and/or pending patent applications are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of a patent or patent application. We have systems in place to remind us to pay these fees, and we employ an outside firm and rely on our outside counsel to pay these fees. While an inadvertent lapse may sometimes be cured by payment of a late fee or by other means in accordance with the applicable rules, there are many situations in which noncompliance 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. If we fail to maintain the patents and patent applications directed to our product or product candidates, our competitors might be able to enter the market earlier than should otherwise have been the case, which would have a material adverse effect on our business.

We may not be able to protect our intellectual property rights throughout the world.

Filing and prosecuting patent applications, and defending patents on our product and product candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly developing countries. For example, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement on infringing activities is inadequate. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to pharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally in those countries. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could

provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. In addition, certain countries in Europe and certain other countries, including India and China, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we may have limited remedies if our patents are infringed or if we are compelled to grant a license to our

patents to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license. Finally, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws.

Third-party claims alleging intellectual property infringement may adversely affect our business.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties, for example, patents and proprietary rights of competitors. Our research, development and commercialization activities, including the commercialization of OTIPRIO, may be subject to claims that we infringe or otherwise violate patents owned or controlled by third parties, including our competitors. There are also patent applications, owned by third parties including competitors, that have been filed but not issued that, if issued as patents, may be asserted against us. Numerous U.S. and foreign issued patents and pending patent applications, exist in the otic field in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our activities related to our product or product candidates may give rise to claims of infringement of the patent rights of third parties. We cannot assure you that our product or product candidates will not infringe existing or future patents owned by third parties. We may not be aware of patents that have already issued and that a third party, for example a competitor in the otic market, might assert are infringed by our product or product candidates. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our product or product candidates, could be found to be infringed by our product or product candidates.

Third parties making claims against us for infringement or misappropriation of their intellectual property rights may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop our product candidates and commercialize our product and product candidates, if approved. Further, if a patent infringement suit were brought against us, we could be forced to stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit. Regardless of the merits of any third-party claims, our defense against such claims, or other related actions we may take, could cause us to incur substantial expenses, and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us by a third party, we may have to (i) pay substantial damages, including treble damages and attorneys' fees if we are found to have willfully infringed the third party's patents; (ii) obtain one or more licenses from the third party; (iii) pay royalties to the third party; and/or (iv) redesign any infringing products. Redesigning any infringing products may be impossible or require substantial time and monetary expenditure. Further, we cannot predict whether any required license would be available at all or whether it would be available on commercially reasonable terms. In the event that we could not obtain a license, we may be unable to further develop our product candidates and commercialize our product and product candidates, if approved, which could harm our business significantly. Even if we are able to obtain a license, the license would likely obligate us to pay license fees or royalties or both, and the rights granted to us might be nonexclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations, if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms.

Engaging in litigation is very expensive, particularly for a company of our size, and time-consuming. Some of our competitors may be able to sustain the costs of litigation or administrative proceedings more effectively than we can because of greater financial resources. Patent litigation and other proceedings may also absorb significant management time. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could impair our ability to compete in the marketplace. The occurrence of any of the foregoing could have a material adverse effect on our business, financial condition or results of operations.

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

Third parties may infringe or misappropriate our intellectual property, including our existing patents, patents that may issue to us in the future, or the patents of our licensors to which we have a license. As a result, we may be required to file infringement claims to stop third-party infringement or unauthorized use. Further, we may not be

able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

Generic drug manufacturers may develop, seek approval for, and launch generic versions of our products. If we file an infringement action against such a generic drug manufacturer, that company may challenge the scope, validity or enforceability of our or our licensors' patents, requiring us and/or our licensors to engage in complex, lengthy and costly litigation or other proceedings. For example, if we or one of our licensors initiated legal proceedings against a third party to enforce a patent covering our product or product candidates, the defendant could counterclaim that the patent covering our product or product candidates is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent.

In addition, within and outside of the United States, there has been a substantial amount of litigation and administrative proceedings, including interference and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in various foreign jurisdictions, regarding patent and other intellectual property rights in the pharmaceutical industry. Recently, the AIA introduced new procedures including inter partes review and post grant review. The implementation of these procedures brings uncertainty to the possibility of challenges to our patents in the future, including challenges to those patents perceived by our competitors as blocking entry into the market for their products, and the outcome of such challenges.

Such litigation and administrative proceedings could result in revocation of our patents or amendment of our patents such that they do not cover our product or product candidates. They may also put our pending patent applications at risk of not issuing, or issuing with limited and potentially inadequate scope to cover our product and product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. Additionally, it is also possible that prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, may, nonetheless, ultimately be found by a court of law or an administrative panel to affect the validity or enforceability of a claim, for example if a priority claim is found to be improper. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product and product candidates. Such a loss of patent protection could have a material adverse impact on our business.

Enforcing our or our licensor's intellectual property rights through litigation is very expensive, particularly for a company of our size, and time-consuming. Some of our competitors may be able to sustain the costs of litigation more effectively than we can because of greater financial resources. Patent litigation and other proceedings may also absorb significant management time. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could impair our ability to compete in the marketplace. The occurrence of any of the foregoing could have a material adverse effect on our business, financial condition or results of operations.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, during the course of litigation or administrative proceedings, there could be public announcements of the results of hearings, motions or other interim proceedings or developments or public access to related documents. If investors perceive these results to be negative, the market price for our common stock could be significantly harmed.

Although it is not expected to be relevant to our product or any of our product candidates, on April 17, 2015, we filed a request for interference between one of our U.S. pending applications and a U.S. pending application controlled by Auris Medical Holding AG (Auris). On July 20, 2015, we received notice from the USPTO that the Patent Trial and

Appeal Board (PTAB) declared an interference between our pending application and the Auris patent (issued as U.S. Patent No. 9,066,865 on June 30, 2015). On January 26, 2017, the PTAB determined that all of Otonomy's patent claims and all but one of the Auris patent claims are not patentable. In addition, the PTAB determined that the written description supporting Auris's single claim is as of Auris's filing date of 2014 rather than the 2005 date argued by Auris. This interference decision does not involve issued U.S. patents covering our product or product candidates. We filed a Notice of Appeal on March 27, 2017, in which we asked the Federal Circuit to reverse PTAB's decision that our claims are not patentable and that Auris's single claim is. On April 5,

2017, Auris filed a Notice of Cross-Appeal to ask the Federal Circuit to reverse PTAB's decision that Auris's other claims are not patentable. The appeal proceedings are ongoing. We continue to monitor patent applications filed and being prosecuted by Auris, in case we may need to consider similar or other actions.

If we fail to comply with our obligations in any of the agreements under which we license intellectual property 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 are a party to a number of license agreements under which we are granted intellectual property rights that are crucial to our business. A portion of our patent portfolio for our product and certain product candidates was co-developed and is co-owned with UC which licensed its rights to us through an exclusive worldwide license agreement. Under our existing license agreement with UC, we are subject to various obligations, including development and commercialization diligence obligations, and patent prosecution and maintenance obligations, as well as financial obligations such as potential development milestone payments, sublicensing income payments, and royalty payments. If we fail to comply with any of these obligations or otherwise breach other terms of our license agreement, and fail to cure such breach, UC may have the right to terminate the license or, in the instance where we fail to meet our diligence obligations, UC may instead elect to change our exclusive license to a non-exclusive license. The loss of the license from UC would affect a significant portion of the patent portfolio for OTIPRIO and OTIVIDEX, as well as certain other product candidates we may develop. While we could still proceed with development and, if approved, commercialization of OTIPRIO, OTIVIDEX and other product candidates as co-owner of the licensed patents, third parties, such as our competitors, could enter into the market by obtaining a license from UC under UC's rights to such patents.

In addition, a portion of our patent portfolio for our OTO-313 product candidate is exclusively in-licensed from DURECT Corporation (Durect), which license includes a sublicense to patents jointly owned by Durect and the Institut National de la Sante et de la Recherche Medicale (INSERM). Under our existing license agreement with Durect, we are subject to various obligations, including development and commercialization diligence obligations and pre-commercial launch progress reporting obligations, as well as financial obligations such as potential development milestone payments, sublicensing income payments, and royalty payments to both Durect and INSERM. If we fail to comply with the diligence obligations or otherwise materially breach our license agreement, and fail to remedy such failure or cure such breach, Durect may have the right to terminate the license or, in the instance of our failure to meet the diligence obligations, Durect may instead elect to convert our exclusive license to a non-exclusive license. In particular, the loss of the license from Durect would affect a portion of the patent portfolio for OTO-313, which would adversely affect our ability to proceed with any development or potential commercialization of OTO-313, and could subject us to claims of patent infringement by Durect if OTO-313 is covered by the licensed patents.

Licensing of intellectual property rights is of critical importance to our business and involves complex legal, business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property rights subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- our right to sublicense intellectual property rights to third parties under collaborative development relationships; and
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product and product candidates, and what activities satisfy those diligence obligations.

While we would expect to exercise all rights and remedies available to us, including seeking to cure any breach by us, and otherwise seek to preserve our rights under the patents licensed to us, we may not be able to do so in a timely manner, at an acceptable cost or at all. Generally, the loss of any one of our current licenses, or any other license we may acquire in the future, could materially harm our business, prospects, financial condition and results of operations.

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We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We have received confidential and proprietary information from third parties. In addition, we employ individuals, consultants and independent contractors who were previously employed at other biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise improperly used or disclosed confidential information of these third parties or their former employers. Further, we may be subject to ownership disputes in the future arising, for example, from conflicting obligations of consultants, independent contractors or others who are involved in developing our product candidates. We may also be subject to claims that former employees, consultants, independent contractors, collaborators or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging our right to and use of confidential and proprietary information. If we fail in defending any such claims, in addition to paying monetary damages, we may lose our rights therein. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees.

Risks Related to Government Regulation

Our business and products are subject to extensive government regulation.

We are subject to extensive, complex, costly and evolving regulation by federal and state governmental authorities in the United States, principally by the FDA, the U.S. Drug Enforcement Administration (DEA), the Centers for Disease Control and Prevention (CDC), the U.S. Department of Health and Human Services, and its various agencies, and also from state and foreign regulatory authorities. Failure to comply with all applicable regulatory requirements, including those promulgated under the Federal Food, Drug, and Cosmetic Act (FFDCA), the Public Health Service Act, and the Controlled Substances Act, among others, may subject us to operating restrictions and criminal prosecution, monetary penalties and other disciplinary actions, including, sanctions, warning letters, product seizures, recalls, fines, injunctions, suspension, revocation of approvals, disgorgement, contractual damages, and/or exclusion from future participation in the Medicare and Medicaid programs. After our products receive regulatory approval or clearance, we, and our direct and indirect suppliers, remain subject to the periodic inspection of our plants and facilities, review of production processes, and testing of our products to confirm that we are in compliance with all applicable regulations. Adverse findings during regulatory inspections may result in the implementation of Risk Evaluation and Mitigation Strategies (REMS), programs, completion of government mandated clinical trials, and government enforcement action relating to labeling, advertising, marketing and promotion, as well as regulations governing cGMPs.

The regulatory approval process is highly uncertain and we may not obtain regulatory approval for the commercialization of OTIVIDEX, OTO-313, OTO-413 or any other product candidates.

The research, testing, manufacturing, labeling, approval, selling, import, export, marketing and distribution of drug products are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, which regulations differ from country to country. We are not permitted to market our product candidates in the United States until we receive approval of an NDA from the FDA. Obtaining regulatory approval of a product can be a lengthy, expensive and uncertain process. In addition, failure to comply with FDA and other applicable United States and foreign regulatory requirements may subject us to administrative or judicially imposed sanctions or other actions, including:

- warning letters and adverse publicity;
- civil and criminal penalties;
- injunctions;

- withdrawal of approved products;
- product seizure or detention;
- product recalls;

- total or partial suspension of production; and
- refusal to approve pending NDAs or supplements to approved NDAs.

Prior to obtaining approval to commercialize a product candidate in the United States or abroad, we must demonstrate with substantial evidence from well-controlled nonclinical studies and clinical trials, and to the satisfaction of the FDA or other foreign regulatory agencies, that such product candidates are safe and effective for their intended uses. Results from nonclinical studies and clinical trials can be interpreted in different ways, and insufficient or adverse results from nonclinical studies can affect the ability to conduct clinical trials. For example, following completion of a Phase 1b clinical trial, the OTIVIDEX program was put on Full Clinical Hold due to adverse findings in a nonclinical study evaluating the safety of repeated doses of OTIVIDEX. OTIVIDEX was subsequently removed from Full Clinical Hold in July 2013, allowing for initiation of the Phase 2b single-dose clinical trial, and placed on Partial Clinical Hold prohibiting the initiation of multiple-dose clinical trials in the United States pending the submission and review of additional nonclinical data. We submitted additional nonclinical data to the FDA and OTIVIDEX was removed from Partial Clinical Hold in June 2014. As a result of OTIVIDEX being placed on Full Clinical Hold, OTIPRIO was also placed on Full Clinical Hold. The OTIPRIO Full Clinical Hold was removed in November 2012. We cannot assure you that our product candidates will not be subject to new clinical holds in the future.

Even if we believe the nonclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. Administering product candidates to humans may produce undesirable side effects, which could interrupt, delay or halt clinical trials and result in the FDA or other regulatory authorities denying approval of a product candidate for any or all targeted indications.

Regulatory approval is not guaranteed, and the approval process is expensive and may take several years. The FDA also has substantial discretion in the approval process. Despite the time and expense expended, failure can occur at any stage, and we could encounter problems that cause us to abandon or repeat clinical trials, or perform additional nonclinical studies and clinical trials. The number of nonclinical studies and clinical trials that will be required for FDA approval varies depending on the product candidate, the disease or condition that the product candidate is designed to address and the regulations applicable to any particular product candidate. The FDA can delay, limit or deny approval of a product candidate for many reasons, including the following:

- a product candidate may not be deemed safe, effective, pure or potent;
- FDA officials may not find the data from nonclinical studies and clinical trials sufficient;
- the FDA might not accept or approve our third-party manufacturers' processes or facilities; or
- the FDA may change its approval policies or adopt new regulations.

If OTIVIDEX, OTO-313, OTO-413 or any other product candidates fail to demonstrate safety and efficacy in clinical trials or do not gain approval, our business and results of operations will be materially and adversely harmed.

For our product, and if we receive regulatory approval for any of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense, or the limiting or withdrawal of regulatory approval and subject us to penalties if we fail to comply with applicable regulatory requirements.

If and when regulatory approval has been granted, our product candidates or any approved product will be subject to continual regulatory review by the FDA and/or non-U.S. regulatory authorities. Additionally, our product and any product candidates, if approved, will be subject to extensive and ongoing regulatory requirements, including labeling and other restrictions and market withdrawal, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products. Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indications for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product. In addition, for our

product, and if the applicable regulatory agency approves our product candidates, the

manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include prompt submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP and GCP for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with our product or our product candidates, including adverse events of unanticipated severity or frequency, or problems with our third-party manufacturers' processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

Our ongoing regulatory requirements may also change from time to time, potentially harming or making costlier our commercialization efforts. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or other countries. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business.

Our relationships with healthcare professionals, clinical investigators, CROs and third-party payors in connection with our current and future business activities may be subject to federal and state healthcare fraud and abuse laws, false claims laws, transparency laws, government price reporting, and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face penalties.

We are subject to various U.S. federal and state health care laws, including those intended to prevent healthcare fraud and abuse.

The federal Anti-Kickback Statute prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare, and Medicaid Remuneration has been broadly defined to include anything of value, including, but not limited to, cash, improper discounts, and free or reduced price items and services. Many states have similar laws that apply to their state health care programs as well as private payors.

Federal false claims laws, including the federal False Claims Act (FCA), and civil monetary penalties law impose penalties against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false or fraudulent or making a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government. The FCA has been used to, among other things, prosecute persons and entities submitting claims for payment that are inaccurate or fraudulent, that are for services not provided as claimed, or for services that are not medically necessary. The FCA includes a whistleblower provision that allows individuals to bring actions on behalf of the federal government and share a portion of the recovery of successful claims. Many states also have similar laws that apply to their state health care programs as well as private payors.

Additionally, state and federal authorities have aggressively targeted medical technology companies for, among other things, alleged violations of these anti-fraud statutes, based on, for example, improper research or

consulting contracts with doctors, certain marketing arrangements that rely on volume-based pricing, off-label marketing schemes, and other improper promotional practices.

The federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), among other things, imposes criminal liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services.

Additionally, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH Act), and their implementing regulations, also imposes certain obligations, including mandatory contractual terms, on certain types of people and entities, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without proper written authorization. Similarly, the collection and use of health data in the EU is governed by the GDPR, which will become fully applicable in May 2018. The GPDR extends the geographical scope of EU Data protection law to non-EU entities under certain conditions, tightens existing EU data protection principles and creates new obligations for companies and new rights for individuals. Failure to comply with the GDPR may result in substantial fines and other administrative penalties. The GDPR may increase our responsibility and liability in relation to personal data that we process and we may be required to put in place additional mechanisms ensuring compliance with the GDPR. This may be onerous and if our efforts to comply with GDPR or other applicable EU laws and regulations are not successful, it could adversely affect our business in the EU.

Since the approval of OTIPRIO, our operations have been subject to the federal transparency requirements under the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to annually report to CMS information related to payments and other transfers of value provided to physicians and teaching hospitals and certain ownership and investment interests held by physicians and their immediate family members.

If any of our business activities, including but not limited to our relationships with healthcare providers or payors, violate any of the aforementioned laws, we may be subject to administrative, civil and/or criminal penalties, damages, monetary fines, disgorgement, individual imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings and curtailment or restructuring of our operations.

In addition, the U.S. Foreign Corrupt Practices Act and similar worldwide anti-bribery laws generally prohibit companies and their intermediaries from making improper payments to non-U.S. officials for the purpose of obtaining or retaining business. We cannot assure you that our internal control policies and procedures will protect us from reckless or negligent acts committed by our employees, future distributors, partners, collaborators or agents. Violations of these laws, or allegations of such violations, could result in fines, penalties or prosecution and have a negative impact on our business, results of operations and reputation.

Legislative or regulatory healthcare reforms in the United States or abroad may make it more difficult and costly for us to obtain regulatory clearance or approval of our product candidates or any future product candidates and to produce, market, and distribute our products after clearance or approval is obtained.

From time to time, legislation is drafted and introduced in Congress in the United States or by governments in foreign jurisdictions that could significantly change the statutory provisions governing the regulatory clearance or approval, manufacture, and marketing of regulated products or the reimbursement thereof. In addition, FDA or foreign regulatory agency regulations and guidance are often revised or reinterpreted by the FDA or the applicable foreign regulatory agency in ways that may significantly affect our business and our product and product candidates. Any new regulations or revisions or reinterpretations of existing regulations may impose additional costs or lengthen review times of our product candidates or any future product candidates. We cannot determine what effect changes in regulations, statutes, legal interpretation or policies, when and if promulgated, enacted or adopted may have on our business in the future. Such changes could, among other things, require:

- changes to manufacturing methods;
- recall, replacement, or discontinuance of one or more of our products; and
- additional recordkeeping.

Each of these would likely entail substantial time and cost and could materially harm our business and our financial results. In addition, delays in receipt of or failure to receive regulatory clearances or approvals for any future products would harm our business, financial condition, and results of operations.

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 have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries with policy limits that we believe are customary for similarly situated companies and adequate to provide us with coverage for foreseeable risks. Although we maintain such insurance, this insurance may not provide adequate coverage against potential liabilities. In addition, 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 research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations which can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, the UK Bribery Act 2010, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. U.S. economic sanctions and export control laws and regulations prohibit the shipment of certain products and services to countries, governments, and persons targeted by U.S. sanctions.

Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other partners from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector.

We may engage third parties for clinical trials outside of the United States, to sell our products abroad once we enter a commercialization phase, and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We also have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We can be held liable for any unauthorized exports and reexports of our products and for the corrupt or other illegal activities of our employees, agents, contractors, and other partners, even if we do not explicitly authorize or have actual knowledge of such activities. Any violation of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

Risks Related to Ownership of Our Common Stock

The market price of our common stock has been and may continue to be volatile, and you could lose all or part of your investment.

Our stock is currently traded on The Nasdaq Global Select Market, but we can provide no assurance that we will be able to maintain an active trading market on The Nasdaq Global Select Market or any other exchange in the future. Moreover, the trading price of our common stock may fluctuate substantially.

The stock market in general and the market for pharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price of our common stock following our initial public offering has been and is likely to continue to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including:

- regulatory or legal developments;
- results from or delays in clinical trials of our product candidates or product candidates of companies that are perceived to be similar to us;
- announcements of regulatory approval or disapproval of our product candidates;
- commercialization of our products;
- FDA or other regulatory actions affecting us or our industry;
- introductions and announcements of new products by us, any commercialization partners or our competitors, and the timing of these introductions and announcements;
- our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- announcements by us or our competitors of significant acquisitions, licenses, strategic partnerships, joint ventures or capital commitments;
- market conditions in the pharmaceutical and biopharmaceutical sectors and issuance of securities analysts' reports or recommendations;
- actual or anticipated quarterly variations in our results of operations or those of our competitors;
- changes in financial estimates or guidance, including our ability to meet our revenue, operating profit or loss and cash balance estimates or guidance;
- sales of substantial amounts of our stock by insiders and large stockholders, or the expectation that such sales might occur;
- general economic, industry and market conditions;

- additions or departures of key personnel;
- intellectual property, product liability or other litigation against us;
- expiration or termination of our potential relationships with strategic partners;
- limited trading volume of our common stock; and
- the other factors described in this "Risk Factors" section.

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

The trading market for our common stock will be influenced in part on the research and reports that equity research analysts publish about us and our business. Although certain equity research analysts currently cover us, we do not have any control of the analysts or the content and opinions included in their reports or whether any such analysts will continue to, or whether new analysts will, cover us for any given period of time. The price of our common stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analyst ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which in turn could cause our stock price or trading volume to decline.

Sales of substantial amounts of our common stock in the public markets, or the perception that such sales might occur, could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. If our stockholders sell, or the market perceives that our stockholders intend to sell, substantial amounts of our common stock in the public market, the market price of our common stock could decline significantly.

As of December 31, 2017, certain holders of approximately 4,192,639 shares of our common stock, including shares issuable upon the exercise of outstanding options, are entitled to certain rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by our affiliates as defined in Rule 144 under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the market price of our common stock.

If we sell shares of our common stock in future financings, stockholders may experience immediate dilution and, as a result, the market price of our common stock may decline.

We may from time to time issue additional shares of common stock at a discount from the current trading price of our common stock. As a result, our stockholders would experience immediate dilution upon the purchase of any shares of our common stock sold at such discount. In addition, as opportunities present themselves, we may enter into financing or similar arrangements in the future, including the issuance of debt securities, preferred stock or common stock. In September 2015, our shelf registration statement on Form S-3 (File No. 333-206752) was declared effective by the SEC, pursuant to which we may offer debt securities, preferred stock, common stock and certain other securities from time to time, and in January 2016 we sold 5,750,000 shares of common stock pursuant to such shelf registration statement. If in the future we issue additional shares of common stock or securities convertible into common stock, our common stockholders would experience additional dilution and, as a result, the market price of our common stock may decline.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law.

In addition, as permitted by Section 145 of the Delaware General Corporation Law, our amended and restated bylaws and our indemnification agreements that we have entered into with our directors and officers provide that:

- We will indemnify our directors and officers for serving us in those capacities, or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful.
- We may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law.
- We are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification.
- We are not obligated pursuant to our amended and restated bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification.
- The rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons.
- We may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

To the extent that a claim for indemnification is brought by any of our directors or officers, it would reduce the amount of funds available for use in our business.

Concentration of ownership of our common stock among our existing principal stockholders may effectively limit the voting power of other stockholders.

As of December 31, 2017, our executive officers, directors and current beneficial owners of 5% or more of our common stock, in aggregate, beneficially owned approximately 44.4% of our outstanding common stock. Accordingly, these stockholders, acting together, may significantly influence all matters requiring stockholder approval, including the election and removal of directors and any merger or other significant corporate transactions. These stockholders may therefore delay or prevent a change of control, even if such a change of control would benefit our other stockholders. The significant concentration of stock ownership may adversely affect the market price of our common stock due to investors' perception that conflicts of interest may exist or arise.

Anti-takeover provisions in our corporate charter documents and under Delaware law could make an acquisition of us more difficult, which could discourage takeover attempts and lead to management entrenchment, and the market price of our common stock may be lower as a result.

Certain provisions in our certificate of incorporation and bylaws may make it difficult for a third party to acquire, or attempt to acquire, control of our company, even if a change in control was considered favorable by you and other stockholders. For example, our board of directors has the authority to issue up to 10,000,000 shares of preferred stock. Our board of directors can fix the price, rights, preferences, privileges, and restrictions of the preferred stock without any further vote or action by our stockholders. The issuance of shares of preferred stock may delay or prevent a change in control transaction. As a result, the market price of our common stock and the voting and other rights of our stockholders may be adversely affected. An issuance of shares of preferred stock may result in the loss of voting control to other stockholders.

Our charter documents contain other provisions that could have an anti-takeover effect, including provisions that:

- establish that our board of directors is divided into three classes, Class I, Class II and Class III, with each class serving staggered three-year terms;

- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- provide that our directors may only be removed for cause;
- eliminate cumulative voting in the election of directors;
- authorize our board of directors to issues shares of preferred stock and determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval;
- provide our board of directors with the exclusive right to elect a director to fill a vacancy or newly created directorship;
- permit stockholders to only take actions at a duly called annual or special meeting and not by written consent;
- prohibit stockholders from calling a special meeting of stockholders;
- require that stockholders give advance notice to nominate directors or submit proposals for consideration at stockholder meetings;
- authorize our board of directors, by a majority vote, to amend the bylaws; and
- require the affirmative vote of at least 66 2/3% or more of the outstanding shares of common stock to amend many of the provisions described above.

In addition, we are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Finally, our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders. These provisions could discourage potential acquisition proposals and could delay or prevent a change in control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that certain investors are willing to pay for our stock.

We may be subject to securities litigation, which is expensive and could divert management attention.

The market price of our common stock has been and will likely continue to be volatile, and in the past companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, will be your sole source of gains.

We have not declared or paid cash dividends on our common stock to date. We currently intend to retain our future earnings, if any, to fund the development and growth of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

Our ability to use our net operating loss carryforwards and certain other tax attributes to offset future taxable income may be subject to certain limitations.

As of December 31, 2017, we had U.S. federal and state net operating loss carryforwards (NOLs) of approximately $241.6 million and $101.3 million, respectively, which expire in various years beginning in 2030, if not utilized. As of December 31, 2017, we had federal and California research and development tax credit carryforwards of approximately $7.9 million and $3.9 million, respectively. The federal research and development tax credit carryforwards expire in various years beginning in 2030, if not utilized. The California research and development credit will carry forward indefinitely. Under Sections 382 and 383 of Internal Revenue Code of 1986, as amended (Code) if a corporation undergoes an "ownership change," the corporation's ability to use its pre-change NOLs and other pre-change tax attributes, such as research tax credits, to offset its future post-change income and

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taxes may be limited. In general, an "ownership change" occurs if there is a cumulative change in our ownership by "5% shareholders" that exceeds 50 percentage points over a rolling three-year period. Similar rules may apply under state tax laws. We believe we have experienced certain ownership changes in the past and have reduced our deferred tax assets related to NOLs and research and development tax credit carryforwards accordingly. In the event that it is determined that we have in the past experienced additional ownership changes, or if we experience one or more ownership changes as a result of future transactions in our stock, then we may be further limited in our ability to use our NOLs and other tax assets to reduce taxes owed on the net taxable income that we earn in the event that we attain profitability. Any such limitations on the ability to use our NOLs and other tax assets could adversely impact our business, financial condition and operating results in the event that we attain profitability.

The recently passed comprehensive tax reform bill could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law new legislation that significantly revises the Internal Revenue Code of 1986, as amended. The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain, and our business and financial condition could be adversely affected. Our net deferred tax assets and liabilities were revalued at the newly-enacted U.S. corporate rate. We do not expect this to have a material impact on our financials because we currently maintain a full valuation allowance on our U.S. deferred tax assets. We continue to examine the impact that this tax reform legislation may have on our business. In addition, it is uncertain if and to what extent various states will conform to the newly enacted federal tax law.

We have incurred and will continue to incur costs as a result of operating as a public company, and our management has been and will continue to be required to devote substantial time to new compliance initiatives and corporate governance practices, including maintaining an effective system of internal control over financial reporting.

As a public company listed in the United States, and increasingly after we are no longer an "emerging growth company," we have incurred and will continue to incur significant additional legal, accounting and other expenses that we did not incur as a private company. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure, including the Sarbanes-Oxley Act and regulations implemented by the SEC, and The NASDAQ Stock Market (NASDAQ) may increase legal and financial compliance costs and make some activities more time consuming. These laws, regulations and standards are subject to varying interpretations and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities. If notwithstanding our efforts to comply with new laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

As a public company in the United States, we are required, pursuant to Section 404 of the Sarbanes-Oxley Act of 2002 (Section 404), to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting. We need to disclose any material weaknesses identified by our management in our internal control over financial reporting, and when we are no longer an "emerging growth company," we will need to provide a statement that our independent registered public accounting firm has issued an opinion on our internal control over financial reporting. Our first report on compliance with Section 404 was furnished in connection with our financial

statements for the year ended December 31, 2015.

The controls and other procedures are designed to ensure that information required to be disclosed by us in the reports that we file with the SEC, is disclosed accurately and is recorded, processed, summarized and reported within the time periods specified in SEC rules and forms. We are in the early stages of conforming our internal control procedures to the requirements of Section 404, and we may not be able to complete our evaluation, testing and any

required remediation needed to comply with Section 404 in a timely fashion. Our independent registered public accounting firm was not engaged to perform an audit of our internal control over financial reporting for the year ended December 31, 2017 or for any other period. Accordingly, no such opinion was expressed in this Annual Report on Form 10-K.

Even after we develop these new procedures, these new controls may become inadequate because of changes in conditions or the degree of compliance with these policies or procedures may deteriorate and material weaknesses in our internal control over financial reporting may be discovered. We may err in the design or operation of our controls, and all internal control systems, no matter how well designed and operated, can provide only reasonable assurance that the objectives of the control system are met. Because there are inherent limitations in all control systems, there can be no absolute assurance that all control issues have been or will be detected. If we are unable, or are perceived as unable, to produce reliable financial reports due to internal control deficiencies, investors could lose confidence in our reported financial information and operating results, which could result in a negative market reaction.

To fully comply with Section 404, we will need to retain additional employees to supplement our current finance staff, and we may not be able to do so in a timely manner, or at all. In addition, in the process of evaluating our internal control over financial reporting, we expect that certain of our internal control practices will need to be updated to comply with the requirements of Section 404 and the regulations promulgated thereunder, and we may not be able to do so on a timely basis, or at all. In the event that we are not able to demonstrate compliance with Section 404 in a timely manner, or are unable to produce timely or accurate financial statements, we may be subject to sanctions or investigations by regulatory authorities, such as the SEC or NASDAQ, and investors may lose confidence in our operating results and the price of our common stock could decline. Furthermore, if we are unable to certify that our internal control over financial reporting is effective and in compliance with Section 404, we may be subject to sanctions or investigations by regulatory authorities, such as the SEC or NASDAQ, and we could lose investor confidence in the accuracy and completeness of our financial reports, which could hurt our business, the price of our common stock and our ability to access the capital markets.

We also expect that being a public company will make it more difficult for us to attract and retain qualified persons to serve on our board of directors, on committees of our board of directors or as members of senior management.

We are an “emerging growth company,” and the reduced disclosure requirements applicable to emerging growth companies could make our common stock less attractive to investors.

We are an “emerging growth company,” as defined in the JOBS Act enacted in April 2012, as amended, and may remain an “emerging growth company” for up to five years following the completion of our initial public offering, or December 31, 2019, although, if we have more than $1.07 billion in annual revenue, the market value of our common stock that is held by non-affiliates exceeds $700 million as of June 30 of any year, or we issue more than $1.0 billion of non-convertible debt over a three-year period before the end of that five-year period, we would cease to be an “emerging growth company” as of the following December 31. For as long as we remain an “emerging growth company,” we are permitted and intend to continue to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not “emerging growth companies.” These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced “Management’s discussion and analysis of financial condition and results of operations” disclosure;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional

information about the audit and the financial statements;

- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards, delaying the adoption of these accounting standards until they would apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and, as a result, we have and will continue to adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies. We cannot predict whether investors will find our common stock less attractive as a result of our reliance on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and the market price of our common stock may be reduced or more volatile.

Item 1B. UNRESOLVED STAFF COMMENTS

None.

Item 2. PROPERTIES

Our corporate headquarters are located in San Diego, California, where we lease and occupy approximately 62,000 square feet of space, which we believe is adequate to meet our existing needs. The current term of our lease on this facility expires in September 2027. We have an option to extend this lease by an additional five years.

Item 3. LEGAL PROCEEDINGS

From time to time, we may be involved in various claims and legal proceedings relating to claims arising out of our operations. We are not currently a party to any legal proceedings that, in the opinion of our management, are likely to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Item 4. MINE SAFETY DISCLOSURE

Not applicable.

PART II

Item 5. MARKET FOR REGISTRANT'S COMMON EQUITY RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information for Common Stock

Our common stock began trading on The NASDAQ Global Select Market under the symbol "OTIC" on August 13, 2014. Prior to that date, there was no public trading market for our common stock. The following table sets forth for the periods indicated the high and low sales price per share of our common stock, as reported on The NASDAQ Global Select Market:

	Price Range	
	High	Low
Year Ended December 31, 2017		
First Quarter	$18.60	$11.70
Second Quarter	$19.25	$11.30
Third Quarter	$21.15	$3.15
Fourth Quarter	$6.30	$2.80
Year Ended December 31, 2016		
First Quarter	$27.23	$12.17
Second Quarter	$17.60	$10.50
Third Quarter	$19.38	$13.46
Fourth Quarter	$19.30	$11.75

Holders of Record

On March 2, 2018, the closing sale price of our common stock on The NASDAQ Global Select Market was $5.70. As of March 2, 2018, there were approximately 26 stockholders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust or by other entities.

Dividend Policy

We have never declared or paid cash dividends on our common stock. We currently intend to retain all available funds and any future earnings for use in the operation of our business and do not anticipate paying any dividends on our common stock in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors and will depend on, among other factors, our financial condition, operating results, capital requirements, general business conditions and other factors that our board of directors may deem relevant.

Securities Authorized for Issuance Under Our Equity Compensation Plans

Information regarding our equity compensation plans is incorporated by reference to Item 12, "Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters" of Part III of this Annual Report on Form 10-K.

Recent Sale of Unregistered Securities

There were no sales of unregistered securities during the period covered by this Annual Report on Form 10-K, other than those previously reported in a Quarterly Report on Form 10-Q or in a Current Report on Form 8-K.

Use of Proceeds

None.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Performance Graph

This performance graph shall not be deemed “soliciting material” or to be “filed” with the SEC for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (Exchange Act), or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any filing of Otonomy, Inc. under the Securities Act of 1933, as amended, or the Exchange Act.

The following graph compares the cumulative total return to stockholders on our common stock relative to the cumulative total returns of the NASDAQ Composite Index and the NASDAQ Biotechnology Index. An investment of $100 (with reinvestment of all dividends) is assumed to have been made in our common stock and in each index on August 13, 2014, the date our common stock began trading on The NASDAQ Global Select Market, and its relative performance is tracked through December 31, 2017. The returns shown are based on historical results and are not intended to suggest future performance.

Item 6. SELECTED FINANCIAL DATA

The following selected historical consolidated financial data should be read in conjunction with Part II, Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations", our consolidated financial statements and the related notes included in Item 8, "Financial Statements and Supplementary Data" of this Annual Report on Form 10-K.

	Years Ended December 31,		
	2017	2016	2015
Statements of Operations Data:			
Product sales, net	$1,236	$683	$—
Costs and operating expenses:			
Cost of product sales	3,098	1,664	—
Research and development	42,701	60,723	38,762
Selling, general and administrative	46,838	49,777	23,214
Total costs and operating expenses	92,637	112,164	61,976
Loss from operations	(91,401)	(111,481)	(61,976)
Other income (expense)	1,271	898	308
Net loss	$(90,130)	$(110,583)	$(61,668)
Net loss per share, basic and diluted	$(2.97)	$(3.69)	$(2.57)
Weighted-average shares used to compute net loss per share, basic and diluted	30,304,158	29,962,781	23,952,562

	As of December 31,		
	2017	2016	2015
Balance Sheets Data:			
Cash and cash equivalents	$18,456	$24,156	$158,664
Short-term investments	101,548	172,222	26,172
Working capital	114,254	186,987	176,864
Total assets	128,364	208,596	193,030
Accumulated deficit	(364,850)	(274,720)	(164,137)
Total stockholders' equity	117,279	192,737	181,534

Item 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with the section entitled "Selected Financial Data" and the financial statements and related notes included elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements based upon current expectations that involve risks and uncertainties. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of various factors, including those discussed in the section entitled "Risk Factors" and in other parts of this Annual Report on Form 10-K.

Overview

We are a biopharmaceutical company dedicated to the development of innovative therapeutics for otology. We pioneered the application of drug delivery technology to the ear in order to develop products that achieve sustained drug exposure from a single local administration. This approach is covered by a broad patent estate and is being utilized to develop a pipeline of products addressing important unmet medical needs including Ménière's disease, hearing loss and tinnitus.

OTIVIDEX^{M} is a steroid in development for the treatment of Ménière's disease. Two Phase 3 trials in Ménière's disease patients were completed in the second half of 2017. The AVERTS-2 trial, conducted in Europe, achieved its primary endpoint (p value = 0.029) while the AVERTS-1 trial, conducted in the United States, did not (p value = 0.62). Based on a recent Type C meeting with the FDA, we believe that one additional successful pivotal trial is sufficient to support the U.S. registration of OTIVIDEX in Ménière's disease. We expect to initiate this trial in mid-2018.

Gacyclidine is a potent and selective NMDA receptor antagonist in development for the treatment of tinnitus. A Phase 1 clinical safety trial has been successfully completed using OTO-311, a poloxamer-based formulation of gacyclidine, with no safety concerns observed. We have shifted development to OTO-313, an alternative formulation of gacyclidine that has improved properties compared to OTO-311. We expect to initiate a Phase 1/2 clinical trial for OTO-313 in tinnitus patients in the first half of 2019.

We are advancing three distinct hearing loss programs that address different pathologies and broad patient populations. OTO-413 is a sustained exposure formulation of BDNF in development for the repair of cochlear synaptopathy and the treatment of speech-in-noise hearing difficulties. We have initiated nonclinical studies and manufacturing for OTO-413 to support an IND Application, with a Phase 1/2 clinical trial expected to begin in hearing loss patients in the first half of 2019. OTO-5XX is an otoprotectant in development for the prevention of CIHL. OTO-6XX induces hair cell regeneration in a nonclinical proof-of-concept model and is being developed for the treatment of severe hearing loss. We expect to select a candidate for clinical development for both the OTO-5XX and OTO-6XX programs in the second half of 2018.

In addition, we developed, received FDA approval, and commercially launched OTIPRIO® (ciprofloxacin otic suspension) for use during TTP surgery in pediatric patients. OTIPRIO was also recently approved by the FDA for the treatment of AOE. In November 2017, we announced the discontinuation of promotional support for OTIPRIO in order to significantly reduce operating expenses related to the product. OTIPRIO continues to be available for purchase by customers while we evaluate commercial partnering options for the product, including divestiture.

We have a limited operating history. Since our inception in 2008, we have devoted substantially all our efforts to developing and commercializing OTIPRIO, developing our current product candidates, and providing general and administrative support for these operations. As of December 31, 2017, we had cash, cash equivalents and short-term

investments of $120.0 million.

We have never been profitable, and as of December 31, 2017, we had an accumulated deficit of $364.9 million. Our net losses were $90.1 million, $110.6 million and $61.7 million for the years ended December 31, 2017, 2016 and 2015, respectively. Substantially all our net losses have resulted from research and development expenses related to our clinical trials and product development activities, commercialization expenses to launch OTIPRIO in the U.S. market, and other general and administrative expenses.

We expect to continue to incur significant expenses and operating losses for the foreseeable future as we continue to develop, seek regulatory approval, and, if approved, commercialize our product candidates. In the near term, we anticipate that our expenses will continue to be substantial as we:

- conduct clinical development of OTIVIDEX;
- conduct nonclinical development of OTO-313 and OTO-413;
- contract to manufacture our product candidates;
- evaluate opportunities for development of additional product candidates;
- maintain and expand our intellectual property portfolio;
- hire additional staff as necessary to execute our product development plan; and
- operate as a public company.

We may require additional financing to complete the development of and, if approved, commercialize, OTIVIDEX, OTO-313, OTO-413 and any other product candidates. We believe that we will continue to expend substantial resources for the foreseeable future for the development of OTIVIDEX, OTO-313, OTO-413 and any other product candidates we may choose to pursue. These expenditures will include costs associated with marketing and selling any products approved for sale, manufacturing, preparing regulatory submissions, and conducting nonclinical studies and clinical trials. The amount and timing of our future funding requirements, if any, will depend on many factors, including the pace and results of our clinical development efforts, the timing and nature of the regulatory approval process for our product candidates, and our ability to effectively find a commercial partner or acquiror for OTIPRIO. If additional financing is required, we anticipate that we will seek funding through public or private equity or debt financings or other sources, such as potential collaboration arrangements. We may not be able to raise capital on terms acceptable to us, or at all. Our failure to raise capital as and when needed could have a negative impact on our financial condition and our ability to pursue our business strategies. We believe that our existing cash and cash equivalents and short-term investments will be sufficient to fund our currently planned operations through at least the next 24 months.

In November 2008, we entered into an exclusive license agreement with the Regents of the University of California, or UC. Under the license agreement, UC granted us an exclusive license under their rights to patents and applications that are co-developed and co-owned with us for the treatment of human otic diseases. Our financial obligations under the license agreement include development and regulatory milestone payments of up to $2.7 million per licensed product, of which $1.9 million has been paid for OTIPRIO, $0.8 million has been paid for OTIVIDEX, and $0.1 million has been paid for OTO-311 (but such milestone payments are reduced by 75% for any orphan indication product), and a low single-digit royalty on net sales by us or our affiliates of licensed products. In addition, for each sublicense we grant we are obligated to pay UC a fixed percentage of all royalties as well as a sliding-scale percentage of non-royalty sublicense fees received by us under such sublicense, with such percentage depending on the licensed product's stage of development when sublicensed to such third party. We have the right to offset a certain amount of third-party royalties, milestone fees or sublicense fees against the foregoing financial obligations, provided such third-party royalties or fees are paid by us in consideration for intellectual property rights necessary to commercialize a licensed product.

In April 2013, we entered into an exclusive license agreement with DURECT Corporation, or Durect, as part of an asset transfer agreement between us and IncuMed LLC, an affiliate of the NeuroSystec Corporation. Under this license agreement, Durect granted us an exclusive, worldwide, royalty-bearing license under Durect's rights to certain patents and applications that cover our OTO-313 product candidate, as well as certain related know-how. Under this license agreement and the asset transfer agreement, we are obligated to make one-time milestone payments of up to $7.5 million for the first licensed product. Upon commercializing a licensed product, we are obligated to pay Durect tiered, low single-digit royalties on annual net sales by us or our affiliates or sublicensees of the licensed products, and we have the right to offset a certain amount of third-party license fees or royalties against such royalty payments to Durect. In addition, each sublicense we grant to a third party is subject to payment to Durect of a low double-digit

percentage of all non-royalty payments we receive under such sublicense. Additionally, we are also obligated to pay the Institut National de la Sante et de la Recherche Medicale, or INSERM, on behalf of Durect, for a low single-digit royalty payment on net sales by us or our affiliates or sublicensees upon

commercialization of the licensed product. The foregoing royalty payment obligation to Durect would continue on a product-by-product and country-by-country basis until expiration or determination of invalidity of the last valid claim within the licensed patents that cover the licensed product, and the payment obligation to INSERM would continue so long as Durect's license from INSERM remains in effect.

Financial Operations Overview

Revenue

In December 2015, OTIPRIO was approved by the FDA for the treatment of pediatric patients with bilateral otitis media with effusion undergoing TTP surgery. In March 2016, we began sales of OTIPRIO in the United States to our network of specialty distributors who fill orders received from hospitals and ambulatory surgery centers who are the primary end user customers of OTIPRIO for use during TTP surgery. In November 2017, we announced that we discontinued promotional support for OTIPRIO. OTIPRIO continues to be available for purchase by customers while we evaluate commercial partnering options for the product, including divestiture.

We recognize revenue on sales of OTIPRIO upon delivery to our distributors. Product sales are recorded net of estimated chargebacks, government rebates and distributor fees.

Prior to March 2016 we had not generated revenue. We do not expect to generate any revenue from any of our product candidates unless and until we obtain regulatory approval and commercialize our products or enter into collaborative agreements with third parties.

Operating Expenses

Cost of product sales

Cost of product sales consists primarily of direct and indirect costs related to the manufacturing of OTIPRIO, including third party manufacturing costs, allocation of overhead costs and royalty payments based on OTIPRIO sales. OTIPRIO inventory values were written down due to the discontinuation of promotional support for the product indicating our expectation that the useful life and ability to recover inventory costs have decreased. Similarly, OTIPRIO manufacturing equipment was impaired. These expenses were recorded in cost of product sales on the statement of operations.

Research and development expenses

Our research and development expenses primarily consist of costs associated with the nonclinical and clinical development of our product candidates and the development of OTIPRIO for additional indications. Our research and development expenses include:

- employee-related expenses, including salaries, benefits, travel and stock-based compensation expense;
- external development expenses incurred under arrangements with third parties, such as fees paid to contract research organizations (CROs) in connection with nonclinical studies and clinical trials, costs of acquiring and evaluating clinical trial data such as investigator grants, patient screening fees, laboratory work and statistical compilation and analysis, and fees paid to consultants and our scientific advisory board;
- costs to acquire, develop and manufacture clinical trial materials, including fees paid to contract manufacturers;
- payments related to licensed product candidates and technologies;
- costs related to compliance with drug development regulatory requirements; and

- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation of leasehold improvements and equipment, and laboratory and other supplies.

We expense our internal and third-party research and development expenses as incurred.

The following table summarizes our research and development expenses (in thousands) for OTIPRIO and our product candidates:

	Years Ended December 31,		
	2017	2016	2015
Third-party development costs:			
OTIPRIO	$2,300	$15,484	$8,923
OTIVIDEX	15,705	22,979	8,892
OTO-311/OTO-313	414	1,550	3,543
OTO-413	926	—	—
Total third-party development costs	19,345	40,013	21,358
Other unallocated internal research and development costs	23,356	20,710	17,404
Total research and development costs	$42,701	$60,723	$38,762

We expect our research and development expenses to continue to be substantial for the foreseeable future as we advance our product candidates through their respective development programs. The process of conducting nonclinical studies and clinical trials necessary to obtain regulatory approval is costly and time consuming. We may never succeed in achieving regulatory approval for our product candidates. The probability of success will be affected by numerous factors, including nonclinical data, clinical data, competition, manufacturing capability and commercial viability. We are responsible for all of the research and development costs for our programs.

Completion dates and completion costs can vary significantly for each of our clinical development programs and are difficult to predict. We therefore cannot estimate with any degree of certainty the costs we will incur in connection with development of our product candidates. We anticipate that we will make determinations as to which programs and product candidates to pursue and how much funding to direct to each program and product candidate on an ongoing basis in response to the results of ongoing and future clinical trials, regulatory developments, and our ongoing assessments as to each current or future product candidate’s commercial potential. We may need to raise substantial additional capital in the future to complete the development of and, if approved, commercialize, our product candidates. We may enter into collaborative agreements in the future in order to conduct clinical trials and gain regulatory approval of our product candidates, particularly in markets outside of the United States. We cannot forecast which programs or product candidates may be subject to future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development plans and overall capital requirements.

The costs of clinical trials may vary significantly over the life of a program owing to the following:

- per patient trial costs;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the number of patients that participate in the trials;
- the number of doses that patients receive;

- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring or other studies requested by regulatory agencies;
- the duration of patient follow-up;
- the phase of development of the product candidate; and
- the efficacy and safety profile of the product candidate.

Selling, general and administrative expenses

Our selling, general and administrative expenses consist primarily of employee-related expenses, including salaries, benefits, travel and stock-based compensation expense, as well as other related costs for our employees and consultants in executive, commercial, administrative, finance and human resource functions. Other general and administrative expenses include facility-related costs not otherwise included in research and development and professional fees for accounting, auditing, tax and legal fees, and other costs associated with obtaining and maintaining our patent portfolio, commercial support activities for OTIPRIO and commercial preparation activities for our product candidates.

We expect our selling, general and administrative expenses to decrease due to the discontinuation of promotional support for OTIPRIO, but continue to be substantial as we support development of our product candidates, and as we incur ongoing expenses related to audit, legal, regulatory, and tax-related services associated with maintaining compliance with stock exchange listing and SEC requirements, director's and officer's liability insurance premiums, and investor relations-related expenses.

Other Income

Other income primarily consists of interest income earned on cash and cash equivalents and short-term investments.

Critical Accounting Policies and Significant Judgments and Estimates

Our financial statements are prepared in accordance with generally accepted accounting principles in the United States of America. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and assumptions, including those related to net product sales, accrued expenses and stock-based compensation. We base our estimates on our historical experience, known trends and events, and various other factors that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 2 to our financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies are most critical to the judgments and estimates used in the preparation of our financial statements.

Revenue Recognition

We recognize revenue when all of the following four criteria are met: (1) persuasive evidence of an arrangement exists; (2) delivery has occurred or services have been rendered; (3) the fee is fixed or determinable; and (4) collectability is reasonably assured. Determination of criteria (3) and (4) are based on management's judgments regarding the nature of the fee charged for products delivered and the collectability of those fees. If the revenue recognition criteria are not met, we defer the recognition of revenue by recording deferred revenue until such time that all criteria are met.

We began selling OTIPRIO during March 2016. We sell OTIPRIO to a limited number of specialty wholesale distributors, and title and risk of loss transfer upon receipt by these distributors. Hospitals and ambulatory surgery centers order OTIPRIO from these distributors, and are the end users of OTIPRIO. We permit product returns from the distributors only if the product is damaged or is shipped or ordered in error. Product returns based on expiry are

not permitted. Product sales are recorded net of estimated chargebacks, government rebates and distributor fees.

We establish reserves for chargebacks, government rebates and distributor fees utilizing a variety of information including specific contractual terms of agreements with customers, historical rebates and chargebacks, our historical and projected payer mix, industry data, sell-through and inventory on-hand information received from

our distributors and changes in the overall marketplace. Reserves are established for these discounts and allowances upon receipt of OTIPRIO by the distributor and are classified as: (i) an allowance against accounts receivable if the amount is payable to the distributor or (ii) an accrued liability if the amount is payable to a party other than the distributor. Allowances against accounts receivable relate to chargebacks and distributor fees and accruals relate primarily to government rebates. Such reserves result in a reduction to revenue.

Chargebacks. We estimate allowances against accounts receivable for chargebacks related to agreements with group purchasing organizations and federal contracts. Under these agreements, we credit distributors a chargeback amount which represents the difference between wholesale acquisition cost and the discounted price at which eligible purchasers purchased from the distributors. At the time of sale, we record estimated chargebacks based on our historical chargeback activity, the projected payer mix, patient population industry data and the identification of entities that purchase OTIPRIO which are eligible for discounted pricing.

Government Rebates. We estimate a rebate liability in connection with a Medicaid Drug Rebate Agreement with the Centers for Medicare & Medicaid Services, which provides a rebate to participating states based on covered purchases of OTIPRIO. At the time of sale, we record estimated Medicaid rebates based on our historical rebate activity, projected payer mix and Medicaid patient population industry data.

Distributor Fees. Our customers are specialty wholesale distributors with whom we have contracted to pay a fee for service based on a percentage of gross product sales. This fee for service is recorded as an allowance against accounts receivable at the time of sale based on the contracted percentage.

Clinical Trial Expense Accruals

As part of the process of preparing our financial statements, we are required to estimate expenses resulting from our obligations under contracts with vendors, clinical research organizations (CROs) and consultants and under clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts vary and may result in payment flows that do not match the periods over which materials or services are provided under such contracts.

Our objective is to reflect the appropriate trial expenses in our financial statements by recording those expenses in the period in which services are performed and efforts are expended. We account for these expenses according to the progress of the trial as measured by patient progression and the timing of various aspects of the trial. We determine accrual estimates through financial models taking into account discussion with applicable personnel and outside service providers as to the progress of trials. During the course of a clinical trial, we adjust the clinical expense recognition if actual results differ from our estimates. We make estimates of accrued expenses as of each balance sheet date based on the facts and circumstances known at that time. Our clinical trial accruals are dependent upon accurate reporting by CROs and other third-party vendors. Although we do not expect our estimates to differ materially from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low for any particular period. For the years ended December 31, 2017, 2016 and 2015 there were no material adjustments to our prior period estimates of accrued expenses for clinical trials.

Recent Accounting Pronouncements

See Note 2 to our financial statements included in Part II, Item 8, “Financial Statements and Supplementary Data,” of this Annual Report on Form 10-K for a description of recent accounting pronouncements applicable to our business.

Other Information

Net Operating Loss and Research and Development Tax Credit Carryforwards

As of December 31, 2017, we had federal and state net operating loss, NOL, carryforwards of $241.6 million and $101.3 million, respectively. Our federal and state NOL carryforwards will begin to expire in 2030, unless we utilize them beforehand. As of December 31, 2017, we also had federal and California research and development tax

credit carryforwards of $7.9 million and $3.9 million, respectively. The federal research and development tax credit carryforwards will begin expiring in 2030 unless we utilize them beforehand. The California research and development tax credit will carry forward indefinitely.

Pursuant to the Code, Sections 382 and 383, our annual use of our NOL and research and development tax credit carryforwards may be limited in the event that a cumulative change in ownership of more than 50% occurs within a three-year period. We have determined that we have experienced ownership changes in the past. We have reduced our deferred tax assets related to our NOL and federal research and development tax credit carryforwards that we expect to expire unused as a result of these ownership changes. We have excluded these tax attributes from our deferred tax assets with a corresponding reduction of the valuation allowance with no net effect on our income tax expense or our effective tax rate. The California research and development tax credits were not limited because these credits carry forward indefinitely. Future ownership changes as a result of shifts in our stock ownership may further limit our ability to utilize our remaining NOL and research and development tax credit carryforwards.

As of December 31, 2017, we had a full valuation allowance against our deferred tax assets.

JOBS Act

On April 5, 2012, the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an “emerging growth company” can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. In other words, an “emerging growth company” can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

Subject to certain conditions set forth in the JOBS Act, as an “emerging growth company,” we intend to rely on certain exemptions and reduced reporting requirements provided by the JOBS Act, including those relating to (i) providing an auditor’s attestation report on our system of internal control over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and (ii) complying with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis.

We will remain an “emerging growth company” until the earliest of (i) the last day of our first fiscal year in which we have total annual gross revenues of $1.07 billion or more, (ii) the date on which we are deemed to be a “large accelerated filer” under the rules of the SEC with at least $700 million of outstanding equity securities held by non-affiliates, (iii) the date on which we have issued more than $1 billion in non-convertible debt during the previous three years, or (iv) the last day of our fiscal year following the fifth anniversary of the date of the completion of our initial public offering, or December 31, 2019.

Results of Operations

Comparison of the Years Ended December 31, 2017 and 2016

The following table sets forth the significant components of our results of operations for the years ended December 31, 2017 and 2016 (in thousands):

	Years Ended December 31,		
	2017	2016	Change
Product sales, net	$1,236	$683	$553
Cost of product sales	3,098	1,664	1,434
Research and development	42,701	60,723	(18,022)
Selling, general and administrative	46,838	49,777	(2,939)
Interest income	1,271	899	372

Product sales, net. In March 2016, we began sales of OTIPRIO in the United States to our network of specialty distributors who fill orders received from hospitals and ambulatory surgery centers, who are the primary end user customers of OTIPRIO for use during TTP surgery. For the years ended December 31, 2017 and 2016, our net product sales represent revenues for OTIPRIO sold to our distributors during this period. Product sales are recorded net of estimated chargebacks, government rebates and distributor fees. We expect revenue to decrease due to the discontinuation of promotional support for OTIPRIO and the possibility of divesting the product in 2018.

Cost of product sales. Cost of product sales for the years ended December 31, 2017 and 2016 is greater than net product sales primarily due to the discontinuation of promotional support for OTIPRIO, which resulted in a write-down of excess inventory of $1.5 million, and an impairment of OTIPRIO manufacturing equipment of $0.4 million.

Research and development expenses. The decrease of $18.0 million in research and development expenses was primarily due to: (i) a $14.0 million decrease in OTIPRO clinical trial and development costs due to completion of our OTIPRIO label expansion trials in AOE and AOMT, the completion of our Phase 3b clinical trial in pediatric patients with a history of otitis media requiring tympanostomy tubes in 2016, and a decrease in OTIPRIO expenses related to manufacturing, which are recorded as cost of product sales since our commercial launch of OTIPRIO; (ii) a $7.3 million decrease in OTIVIDEX clinical trial and development costs due to the completion and early termination of our OTIVIDEX clinical trials in 2017 and the completion of nonclinical studies and reduced expenses related to manufacturing; and (iii) a $1.1 million decrease in OTO-311 clinical trial and development costs due to the completion of the Phase 1 clinical trial in 2017 and the completion of nonclinical studies. These decreases were partially offset by: (i) a $1.2 million increase related to the cost of filing our sNDA for AOE; (ii) a $0.3 million increase in research costs for our sensorineural hearing loss programs; (iii) a $1.9 million increase in laboratory costs and facilities expense primarily due to the lease of our new headquarters facility, which began in December 2016; and (iv) a $1.0 million increase in personnel costs, including stock-based compensation expense, due to additional headcount.

Selling, general and administrative expenses. The decrease of $2.9 million in selling, general and administrative expenses was primarily related to reduced employee-related expenses of approximately $4.3 million, resulting from reductions in personnel during 2017. These reduced employee-related expenses are net of one-time termination benefits expense. This overall decrease was partially offset by a $1.4 million increase in outside services and facilities expense primarily due to the lease of our new headquarters facility which began in December 2016.

Interest income. Interest income consists primarily of interest earned on our available-for-sale securities. The increase of $0.4 million in interest income was primarily the result of increased available-for-sale securities balances during the year ended December 31, 2017 compared to the year ended December 31, 2016.

Comparison of the Years Ended December 31, 2016 and 2015

The following table sets forth the significant components of our results of operations for the years ended December 31, 2016 and 2015 (in thousands):

	Years Ended December 31,		
	2016	2015	Change
Product sales, net	$683	$—	$683
Cost of product sales	1,664	—	1,664

Research and development	60,723	38,762	21,961
General and administrative	49,777	23,214	26,563
Interest income	899	419	480

Product sales, net. In March 2016, we began sales of OTIPRIO in the United States to our network of specialty distributors who fill orders received from hospitals and ambulatory surgery centers, who are the primary end user customers of OTIPRIO for use during TTP surgery. For the year ended December 31, 2016, our net product sales represented revenues for OTIPRIO sold to our distributors during this period. Product sales were recorded net of estimated chargebacks, government rebates and distributor fees. There were no product sales in 2015.

Cost of product sales. Cost of product sales for the year ended December 31, 2016 was greater than net product sales for this period primarily due to fixed costs associated with manufacturing the initial commercial lots, costs of subsequent commercial validation lots of OTIPRIO available for sale and a write down of excess inventory. There were no product sales in 2015.

Research and development expenses. The increase of $22.0 million in research and development expenses was primarily due to: (i) a $14.0 million increase in OTIVIDEX expenses, which was primarily related to the Phase 3 clinical trial program initiated in November 2015; (ii) a $7.4 million increase in OTIPRIO expenses, which was primarily related to the November 2015 initiation of our OTIPRIO open-label Phase 3b clinical trial in pediatric patients with a history of otitis media requiring tympanostomy tubes and for OTIPRIO label expansion trials in AOE (initiated during June 2016) and AOMT (initiated during March 2016); (iii) a $3.6 million increase in personnel costs, including stock-based compensation expense and overhead, due to additional headcount; and (iv) an impairment charge of $0.6 million to long-lived assets as a result of OTIVIDEX manufacturing equipment expected to be used in research and development which had no future use for the Company. These increases were partially offset by: (i) a $2.1 million decrease in development expenses related to OTO-311; (ii) a $1.0 million decrease in OTIPRIO-related expenses due to the $1.0 million regulatory milestone which was met when we submitted the OTIPRIO NDA to the FDA in February 2015; and (iii) a $0.5 million decrease in OTIVIDEX-related expenses due to the $0.5 million regulatory milestone which was met when we initiated Phase 3 clinical trials in OTIVIDEX in November 2015. There were no regulatory milestone payments incurred during the year ended December 31, 2016.

General and administrative expenses. The increase of $26.6 million in selling, general and administrative expenses was primarily related to the expansion of our operating activities and costs related to the commercial launch of OTIPRIO. The overall increase was comprised of a $21.9 million increase in personnel costs, including stock-based compensation expense and overhead, due to additional headcount, and a $4.7 million increase in expenses for outside services, including OTIPRIO launch costs, travel, consulting costs, legal fees, accounting fees, corporate development and market research.

Interest income. Interest income consists primarily of interest earned on our available-for-sale securities. The increase in interest income was primarily the result of increased available-for-sale securities balances during the year ended December 31, 2016 compared to the year ended December 31, 2015.

Liquidity and Capital Resources

We have incurred significant losses and negative cash flows from operations since our inception. As of December 31, 2017, we had an accumulated deficit of $364.9 million and we expect to continue to incur significant losses for the foreseeable future. We expect our research and development and selling, general and administrative expenses to continue to be substantial for the foreseeable future and, as a result, we may need additional capital to fund our operations, which we may obtain through one or more public or private equity or debt financings, or other sources such as potential collaboration arrangements.

As of December 31, 2017, we had cash, cash equivalents and short-term investments of $120.0 million. We have principally financed our operations through sales and issuances of our equity securities as well as private placements of redeemable convertible preferred stock and convertible notes.

The following table sets forth a summary of the primary sources and uses of cash for the years ended December 31, 2017, 2016 and 2015 (in thousands):

	Years Ended December 31,		
	2017	2016	2015
Net cash (used in) provided by:			
Operating activities	$(75,307)	$(94,305)	$(49,896)
Investing activities	68,998	(149,417)	(11,981)
Financing activities	1,070	109,216	81,426
Net (decrease) increase in cash, cash equivalents and restricted cash	(5,239)	(134,506)	19,549

Operating activities. The primary uses of cash were to fund increased levels of development activities for our product candidates and to support the commercialization of OTIPRIO. We expect to continue the use of cash for development of our product candidates for the foreseeable future.

During the year ended December 31, 2017, we used cash in operating activities of $75.3 million, while our net loss was $90.1 million. The $14.8 million difference consisted of $19.5 million of non-cash adjustments, primarily comprised of stock-based compensation expense, offset by a $4.7 million net change in our operating assets and liabilities.

During the year ended December 31, 2016, we used cash in operating activities of $94.3 million, while our net loss was $110.6 million. The difference consisted of $15.4 million of non-cash adjustments, primarily comprised of stock-based compensation expense, together with a $0.9 million net change in our operating assets and liabilities.

During the year ended December 31, 2015, we used cash in operating activities of $49.9 million, while our net loss was $61.7 million. The difference consisted of $8.7 million of non-cash adjustments, primarily comprised of stock-based compensation expense, a non-cash license fee and depreciation and amortization expense, together with a $3.1 million net change in our operating assets and liabilities.

Investing activities. The primary source of cash from investing activities during the year ended December 31, 2017 was from the maturities of short-term investments. During the year ended December 31, 2017, $129.3 million was used to purchase short-term investments and $1.3 million was used for capital expenditures, which were partially offset by $199.6 million provided by maturities of short-term investments.

Net cash used in investing activities was $149.4 million during the year ended December 31, 2016. During the year ended December 31, 2016, $261.2 million was used to purchase short-term investments and $2.5 million was used for capital expenditures, which were partially offset by $114.3 million provided by maturities of short-term investments.

Net cash used in investing activities was $12.0 million during the year ended December 31, 2015. During the year ended December 31, 2015, $41.3 million was used to purchase short-term investments and $2.0 million was used for capital expenditures, which were partially offset by $31.3 million provided by maturities of short-term investments.

Financing activities. Net cash provided by financing activities was $1.1 million for the year ended December 31, 2017. During the year ended December 31, 2017, proceeds from financing activities were $1.1 million for shares issued for stock option exercises and under our employee stock purchase plan.

Net cash provided by financing activities was $109.2 million for the year ended December 31, 2016. During the year ended December 31, 2016, proceeds from our public offering of common stock completed in January 2016 were $107.6 million after deducting underwriting discounts, commissions and offering-related transaction costs, and other proceeds from financing activities were $1.6 million for shares issued for stock option exercises and under our employee stock purchase plan.

Net cash provided by financing activities was $81.4 million for the year ended December 31, 2015. During the year ended December 31, 2015, proceeds from our follow-on public offering were $80.0 million after deducting underwriting discounts, commissions and offering-related transaction costs, and other proceeds from financing activities were $1.4 million for shares issued for stock option exercises and under our employee stock purchase plan.

Funding Requirements

We expect to continue to incur significant losses for the foreseeable future as we: (i) develop and seek regulatory approvals for our product candidates OTIVIDEX, OTO-313, and OTO-413; and (ii) work to develop additional product candidates through research and development programs. We are subject to all of the risks incident in the development of new therapeutic products, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business.

We believe that our existing cash and cash equivalents and short-term investments will be sufficient to fund our currently planned operations through at least the next 24 months.

We may require additional financing to complete the development of and, if approved, commercialize OTIVIDEX, OTO-313, OTO-413 and any other product candidates. If additional financing is required, we anticipate that we will seek funding through public or private equity or debt financings or other sources, such as potential collaboration arrangements. We may not be able to raise capital on terms acceptable to us, or at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates. If we raise additional funds through the issuance of additional debt or equity securities, it could result in dilution to our existing stockholders, increased fixed payment obligations and the existence of securities with rights that may be senior to those of our common stock. If we incur indebtedness, we could become subject to covenants that would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Any collaboration agreements we enter into may provide capital in the near-term but limit our potential cash flow and revenue in the future. Any of the foregoing could significantly harm our business, financial condition and prospects.

Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. The amount and timing of future funding requirements, both near- and long-term, will depend on many factors, including:

- the revenue generated by OTIPRIO and our product candidates if approved;
- the costs related to manufacturing commercial supplies of OTIPRIO;
- the timing and costs of completing the remaining clinical development and obtaining regulatory approval for OTIVIDEX in Ménière's disease;
- the design, initiation, progress, size, timing, costs and results of nonclinical studies and clinical trials for our other product candidates, including OTO-313 and OTO-413;
- the outcome, timing and cost of regulatory approvals by the FDA and comparable foreign regulatory authorities, including the potential for the FDA or comparable foreign regulatory authorities to require that we perform more studies than, or evaluate clinical endpoints other than, those that we currently expect;
- the timing and costs associated with manufacturing our product candidates for clinical trials, nonclinical studies and for commercial sale;
- the cost of building and maintaining sales, marketing and distribution capabilities for any products for which we may receive regulatory approval and commercialize, including related facilities expansion costs;
- the number and characteristics of product candidates that we pursue;
- the potential acquisition and in-licensing of other technologies, products or assets;
- the extent to which we are required to pay milestone or other payments under our in-license agreements and the timing of such payments;
- the cost of preparing, filing, prosecuting, maintaining, defending and enforcing any patent claims and other intellectual property rights, including litigation costs and the outcome of such litigation;
- our need to expand our development activities, including our need and ability to hire and adequately compensate additional employees;
- the costs associated with being a public company;

- the effect of competing technological and market developments; and
- the cost of litigation, including potential patent litigation.

If we cannot expand our operations or otherwise capitalize on our business opportunities because we lack sufficient capital, our business, financial condition and results of operations could be materially adversely affected.

Off-Balance Sheet Arrangements

During the periods presented we did not have, nor do we currently have, any off-balance sheet arrangements as defined under the applicable rules of the SEC.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2017 that will affect our future liquidity (in thousands):

	Less Than 1 Year	1-3 Years	3-5 Years	More Than 5 Years	Total
	(in thousands)				
Facility operating lease obligations	$2,985	$ 6,000	$ 6,365	$ 16,718	$32,068
Other operating lease obligations	49	87	—	—	136
Other contractual obligations	25	1	—	—	26
Total contractual obligations	$3,059	$ 6,088	$ 6,365	$ 16,718	$32,230

We have payment obligations under license agreements that are contingent upon future events such as our achievement of specified development, regulatory and commercial milestones and are required to make development milestone payments and royalty payments in connection with the sale of products developed under these agreements. As of December 31, 2017, we were unable to forecast with any degree of certainty the timing or likelihood of achieving the milestones or the amounts of future product sales and, therefore, any related payments are not included in the table above.

Item 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Sensitivity

As of December 31, 2017, we had cash and cash equivalents and short-term investments of $120.0 million which are comprised of cash in checking and savings accounts, money market funds, U.S. Treasury securities, certificates of deposit and U.S. government sponsored enterprise securities. The primary objective of our investment activities is to preserve principal and liquidity while maximizing income without significantly increasing risk. We do not enter into investments for trading or speculative purposes. We do not believe that an immediate 10% increase in interest rates would have a material effect on the fair market value of our portfolio, and therefore, we do not expect our operating results or cash flows to be materially affected to any degree by a sudden change in market interest rates.

Foreign Currency Exchange Rate Risk

To date, the vast majority of our contractual obligations have been denominated in U.S. dollars; however, we have contracts with CROs and investigational sites in countries within the European Union and are subject to fluctuations in foreign currency rates in connection with such contracts. In the future, we may contract with other CROs and investigational sites in foreign countries. We do not hedge our foreign currency exchange rate risk. To date, we have not incurred any material effects from foreign currency changes in connection with such contracts.

Inflation

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

Item 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Otonomy, Inc.

Index to Financial Statements

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of Otonomy, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Otonomy, Inc. (the Company) as of December 31, 2017 and 2016, and the related statements of operations, comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2017, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2017, in conformity with U.S. generally accepted accounting principles.

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 audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the 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 audits 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 audits 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 audits 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 audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2010.

San Diego, California

March 8, 2018

Otonomy, Inc.

Balance Sheets

(in thousands, except share and per share data)

	December 31, 2017	2016
Assets		
Current assets:		
Cash and cash equivalents	$18,456	$24,156
Short-term investments	101,548	172,222
Accounts receivable, net	107	91
Inventory	6	1,435
Prepaid and other current assets	2,328	4,316
Total current assets	122,445	202,220
Restricted cash	1,158	697
Property and equipment, net	4,679	4,977
Other long-term assets	82	702
Total assets	$128,364	$208,596
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$961	$1,292
Accrued expenses	3,881	9,064
Accrued compensation	3,307	4,839
Current portion of deferred rent	42	38
Total current liabilities	8,191	15,233
Deferred rent, net of current portion	2,894	626
Total liabilities	11,085	15,859
Commitments and Contingencies		
Stockholders' equity:		
Preferred stock, $0.001 par value, 10,000,000 shares authorized at December 31, 2017 and 2016; no shares issued or outstanding at December 31, 2017 and 2016	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized at December 31, 2017 and 2016; 30,558,726 and 30,255,339 shares issued and outstanding at December 31, 2017 and 2016, respectively	31	30
Additional paid-in capital	482,198	467,468
Accumulated other comprehensive loss	(100)	(41)
Accumulated deficit	(364,850)	(274,720)
Total stockholders' equity	117,279	192,737
Total liabilities and stockholders' equity	$128,364	$208,596

See accompanying notes.

Otonomy, Inc.

Statements of Operations

(in thousands, except share and per share data)

	Years Ended December 31,		
	2017	2016	2015
Product sales, net	$1,236	$683	$—
Costs and operating expenses:			
Cost of product sales	3,098	1,664	—
Research and development	42,701	60,723	38,762
Selling, general and administrative	46,838	49,777	23,214
Total costs and operating expenses	92,637	112,164	61,976
Loss from operations	(91,401)	(111,481)	(61,976)
Other income, net:			
Interest income	1,271	899	419
Other expense	—	(1)	(111)
Total other income, net	1,271	898	308
Net loss	(90,130)	(110,583)	(61,668)
Net loss per share, basic and diluted	$(2.97)	$(3.69)	$(2.57)
Weighted-average shares used to compute net loss per share, basic and diluted	30,304,158	29,962,781	23,952,562

See accompanying notes.

Otonomy, Inc.

Statements of Comprehensive Loss

(in thousands)

	Years Ended December 31,		
	2017	2016	2015
Net loss	$(90,130)	$(110,583)	$(61,668)
Other comprehensive loss:			
Unrealized loss on available-for-sale securities	(59)	(41)	—
Comprehensive loss	$(90,189)	$(110,624)	$(61,668)

See accompanying notes.

Otonomy, Inc.

Statements of Stockholders' Equity

(in thousands, except share data)

	Common Stock Shares	Amount	Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
Balance at December 31, 2014	21,173,270	$ 21	$ 256,061	$ -	$ (102,469)	$ 153,613
Issuance of common stock in public offering	2,932,500	3	80,010	—	—	80,013
Issuance of common stock upon exercise of stock options, net of early exercise liability	174,411	—	680	—	—	680
Issuance of common stock under employee stock purchase plan	49,168	—	718	—	—	718
Issuance of common stock upon exercise of warrants	1,053	—	15	—	—	15
Stock-based compensation expense	—	—	7,716	—	—	7,716
Non-cash license fee	—	—	447	—	—	447
Net loss	—	—	—	—	(61,668)	(61,668)
Balance at December 31, 2015	24,330,402	24	345,647	—	(164,137)	181,534
Issuance of common stock in public offering	5,750,000	6	107,603	—	—	107,609
Issuance of common stock upon exercise of stock options, net of early exercise liability	80,119	—	366	—	—	366
Issuance of common stock under employee stock purchase plan	94,818	—	1,241	—	—	1,241
Stock-based compensation expense	—	—	12,611	—	—	12,611
Net loss	—	—	—	—	(110,583)	(110,583)
Unrealized loss on available-for-sale securities	—	—	—	(41)	—	(41)
Balance at December 31, 2016	30,255,339	30	467,468	(41)	(274,720)	192,737
	191,106	1	447	—	—	448

Issuance of common stock upon exercise of stock options						
Issuance of common stock under employee stock purchase plan	80,072	—	622	—	—	622
Issuance of common stock upon exercise of warrants	32,209	—	—	—	—	—
Stock-based compensation expense	—	—	13,661	—	—	13,661
Net loss	—	—	—	—	(90,130)	(90,130)
Unrealized loss on available-for-sale securities	—	—	—	(59)	—	(59)
Balance at December 31, 2017	30,558,726	$ 31	$ 482,198	$ (100)	$ (364,850)	$ 117,279

See accompanying notes.

Otonomy, Inc.,

Statements of Cash Flows

(in thousands)

	Years Ended December 31,		
	2017	2016	2015
Cash flows from operating activities:			
Net loss	$(90,130)	$(110,583)	$(61,668)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	1,289	708	358
Stock-based compensation	13,661	12,611	7,716
Non-cash license fee	—	—	447
Loss on disposal of assets	—	—	110
Reserve for excess and obsolete inventory	1,546	304	—
Amortization of discount or premium on short-term investments	358	780	13
Impairment of property, plant and equipment	400	602	—
Deferred rent	2,272	358	86
Changes in operating assets and liabilities:			
Accounts receivable, net	(16)	(91)	—
Inventory	153	(1,739)	—
Prepaid and other assets	2,608	(613)	(2,243)
Accounts payable	(398)	(2,158)	1,659
Accrued expenses	(5,518)	3,866	1,012
Accrued compensation	(1,532)	1,650	2,614
Net cash used in operating activities	(75,307)	(94,305)	(49,896)
Cash flows from investing activities:			
Purchases of short-term investments	(129,308)	(261,242)	(41,332)
Maturities of short-term investments	199,565	114,371	31,370
Purchases of property and equipment	(1,259)	(2,546)	(2,019)
Net cash provided by (used in) investing activities	68,998	(149,417)	(11,981)
Cash flows from financing activities:			
Proceeds from issuance of common stock, net of transaction costs	448	108,850	80,731
Proceeds from exercise of stock options, net of early exercise liability	622	366	680
Proceeds from exercise of common stock warrants	—	—	15
Net cash provided by financing activities	1,070	109,216	81,426
Net change in cash, cash equivalents and restricted cash	(5,239)	(134,506)	19,549
Cash, cash equivalents and restricted cash at beginning of period	24,853	159,359	139,810
Cash, cash equivalents and restricted cash at end of period	$19,614	$24,853	$159,359
Supplemental disclosure of non-cash investing and financing activities:			
Purchase of property and equipment in accounts payable and	$132	$647	$286

accrued expenses			
Deferred public offering costs in accounts payable and accrued expenses	$—	$—	$288

See accompanying notes.

Otonomy, Inc.,

Notes to Financial Statements

1. Description of Business and Basis of Presentation

Description of Business

Otonomy, Inc. (Otonomy, the Company or Management) was incorporated in the state of Delaware on May 6, 2008. Otonomy is a biopharmaceutical company dedicated to the development of innovative therapeutics for otology. The Company pioneered the application of drug delivery technology to the ear in order to develop products that achieve sustained drug exposure from a single local administration. OTIVIDEX™ is a steroid formulation that has completed two Phase 3 trials for the treatment of Ménière's disease. OTO-313 is a formulation of the potent and selective N-Methyl-D-Aspartate (NMDA) receptor antagonist gacyclidine that is in development for the treatment of tinnitus. Otonomy is also advancing three preclinical-stage programs that address different pathologies of hearing loss: OTO-413 is a formulation of brain-derived neurotrophic factor (BDNF) for the repair of cochlear synaptopathy and the treatment of speech-in-noise hearing difficulties; OTO-5XX is an otoprotectant for the prevention of cisplatin-induced hearing loss; and OTO-6XX induces hair cell regeneration for the treatment of severe hearing loss.

In addition, the Company developed, received FDA approval, and commercially launched OTIPRIO® (ciprofloxacin otic suspension) for use during tympanostomy tube placement (TTP) surgery in pediatric patients. OTIPRIO was also recently approved by the FDA for the treatment of acute otitis externa (AOE). In November 2017, the Company announced the discontinuation of promotional support for OTIPRIO and its intention to evaluate commercial partnering options for the product, including divestiture.

In January 2016, the Company completed a public offering of 5,750,000 shares of its common stock, which includes the exercise in full by the underwriters of their option to purchase 750,000 shares of common stock, at an offering price of $20.00 per share. Proceeds from the follow-on public offering were approximately $107.6 million, net of underwriting discounts, commissions and offering-related transaction costs.

Basis of Presentation

The financial statements have been prepared assuming the Company will continue as a going concern, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. The Company has incurred operating losses and negative cash flows from operating activities since inception. As of December 31, 2017, the Company had cash, cash equivalents and short-term investments of $120.0 million and an accumulated deficit of $364.9 million. The Company anticipates that it will continue to incur net losses into the foreseeable future as it: (i) continues its development of OTIPRIO for additional indications; (ii) develops and seeks regulatory approvals for OTIVIDEX and its other potential product candidates; and (iii) works to develop additional product candidates through research and development programs. If additional financing is required, the Company anticipates that it will seek additional funding through future debt and/or equity financings or other sources, such as potential collaboration agreements. If the Company is not able to secure adequate additional funding, if or when necessary, the Company may be forced to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible, and/or suspend or curtail planned programs. Any of these actions could materially harm the Company's business, results of operations, and future prospects.

2. Summary of Significant Accounting Policies

Use of Estimates

The financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (GAAP). The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expense during the reporting period. Although these estimates are based on the Company's knowledge of current events and anticipated actions it may undertake in the future, actual results may ultimately materially differ from these estimates and assumptions.

Segment Reporting

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker in making decisions regarding resource allocation and assessing performance. The Company views its operations and manages its business in one operating segment.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of cash, cash equivalents and short-term investments. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits. The Company has not experienced any losses in such accounts and believes it is not exposed to significant risk on its cash balances due to the financial position of the depository institution in which those deposits are held. Additionally, the Company established guidelines regarding approved investments and maturities of investments, which are designed to maintain safety and liquidity.

Cash, Cash Equivalents and Restricted Cash

Cash and cash equivalents consist of cash and highly liquid investments with original maturities of three months or less at the date of purchase. The carrying amounts approximate fair value due to the short maturities of these instruments. Cash and cash equivalents include cash in readily available checking, savings and money market accounts, as well as certificates of deposit.

The Company’s restricted cash consists of cash maintained in separate deposit accounts to secure a letter of credit issued by a bank to the landlord under a lease agreement for the Company’s corporate headquarters (see Note 6 – Commitments and Contingencies for details of the Company’s lease) and to secure the Company’s credit cards.

The following table provides a reconciliation of cash and restricted cash, reported within the balance sheets that sum to the total of the same such amounts in the statements of cash flows as of December 31, (in thousands):

	2017	2016
Cash and cash equivalents	$18,456	$24,156
Restricted cash	1,158	697
Total cash, cash equivalents and restricted cash	$19,614	$24,853

Short-Term Investments

The Company carries short-term investments classified as available-for-sale at fair value as determined by prices for identical or similar securities at the balance sheet date. Short-term investments consist of both Level 1 and Level 2 financial instruments in the fair value hierarchy (as more fully described in Note 7 – Fair Value).

Realized gains or losses of available-for-sale securities are determined using the specific identification method and net realized gains and losses are included in interest income. The Company periodically reviews available-for-sale securities for other-than temporary declines in fair value below the cost basis, and whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. The Company records unrealized gains and losses as a component of other comprehensive loss within the statements of comprehensive loss and as a

separate component of stockholders' equity on the balance sheets.

Fair Value of Financial Instruments

The carrying value of the Company's cash and cash equivalents, short-term investments, prepaid expenses and other current assets, other long-term assets, accounts payable, accrued expenses, and accrued compensation approximate fair value due to the short-term nature of these items.

Accounts Receivable.

Accounts receivable are recorded net of customer allowances for chargebacks, distributor fees and any allowance for doubtful accounts. The Company estimates the allowance for doubtful accounts based on existing contractual payment terms, actual payment patterns of its customers and individual customer circumstances. To date, the Company has determined that an allowance for doubtful accounts is not required.

Inventory

Inventory, which is stated at the lower of cost or market (net realizable value), is based on actual cost in a manner that approximates the first-in, first-out method. Inventories consist of OTIPRIO finished goods and work in-process, as well as raw materials used in the manufacture of OTIPRIO. If inventory costs exceed expected market value due to obsolescence, expiry or quantities in excess of expected demand, write downs are recorded for the difference between cost and market value, less cost to sell. During the year ended December 31, 2017, inventory was nearly completely written down to reflect the discontinuation of promotional support for OTIPRIO and the limited remaining shelf-life on OTIPRIO finished goods, work-in-process and raw materials inventory.

Property and Equipment

Property and equipment generally consist of laboratory equipment, manufacturing equipment, computers and software, and office furniture and are recorded at cost and depreciated using the straight-line method over the estimated useful lives of the assets (generally two to ten years). Leasehold improvements are stated at cost and are depreciated on a straight-line basis over the lesser of the remaining term of the related lease or the estimated useful lives of the assets. Repairs and maintenance costs are charged to expense as incurred.

Impairment of Long-Lived Assets

The Company assesses the value of its long-lived assets, which consist of property and equipment, for impairment on an annual basis and whenever events or changes in circumstances and the undiscounted cash flows generated by those assets indicate that the carrying amount of such assets may not be recoverable. While the Company’s current and historical operating losses and negative cash flows are indicators of impairment, management believes that future cash flows to be received support the carrying value of its long-lived assets. During the year ended December 31, 2017, the Company recorded an impairment of its long-lived assets of approximately $0.4 million in cost of product sales in connection with the OTIPRIO restructurings as more fully described in Note 5 – Restructuring Charges. During the year ended December 31, 2016, the Company recorded an impairment to its long-lived assets of approximately $0.6 million, which is classified within research and development expense on the statements of operations. This impairment was a result of manufacturing equipment expected to be used in research and development which has no future use for the Company. No impairment of long-lived assets were recorded during the year ended December 31, 2015.

Clinical Trial Expense Accruals

As part of the process of preparing the Company’s financial statements, the Company is required to estimate expenses resulting from the Company’s obligations under contracts with vendors, clinical research organizations and consultants and under clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts.

The Company’s objective is to reflect the appropriate clinical trial expenses in its financial statements by recording those expenses in the period in which services are performed and efforts are expended. The Company accounts for these expenses according to the progress of the trial as measured by patient progression and the timing of various aspects of the trial. The Company determines accrual estimates through financial models taking into account discussion with applicable personnel and outside service providers as to the progress or state of its trials. During the course of a clinical trial, the Company adjusts its clinical expense if actual results differ from its estimates, to date, there have not been any material changes to the estimates.

Revenue Recognition

The Company recognizes revenue when all of the following four criteria are met: (1) persuasive evidence of an arrangement exists; (2) delivery has occurred or services have been rendered; (3) the fee is fixed or determinable; and (4) collectability is reasonably assured. Determination of criteria (3) and (4) are based on management's judgments regarding the nature of the fee charged for products delivered and the collectability of those fees. If the revenue recognition criteria are not met, the Company defers the recognition of revenue by recording deferred revenue until such time that all criteria are met.

The Company began selling OTIPRIO in March 2016. The Company sells OTIPRIO to a limited number of specialty wholesale distributors, and title and risk of loss transfer upon receipt by these distributors. Hospitals and ambulatory surgery centers order OTIPRIO from these distributors, and are the end users of OTIPRIO. The Company permits product returns from the distributors only if the product is damaged or is shipped or ordered in error. Product returns based on expiry are not permitted. Product sales are recorded net of estimated chargebacks, government rebates and distributor fees.

The Company establishes reserves for chargebacks, government rebates and distributor fees utilizing a variety of information including specific contractual terms of agreements with customers, historical rebates and chargebacks, the Company's historical and projected payer mix, industry data, sell-through and inventory on-hand information received from the Company's distributors and changes in the overall marketplace. Reserves are established for these discounts and allowances upon receipt of OTIPRIO by the distributor and are classified as: (i) an allowance against accounts receivable if the amount is payable to the distributor or (ii) an accrued liability if the amount is payable to a party other than the distributor. Allowances against accounts receivable relate to chargebacks and distributor fees and accruals relate primarily to government rebates. Such reserves result in a reduction to revenue.

Chargebacks. The Company estimates allowances against accounts receivable for chargebacks related to agreements with group purchasing organizations and federal contracts. Under these agreements, the Company credits distributors a chargeback amount which represents the difference between wholesale acquisition cost and the discounted price at which eligible purchasers purchased from the distributors. At the time of sale, the Company records estimated chargebacks based on the Company's historical chargeback activity, the projected payer mix, patient population industry data and the identification of entities that purchase OTIPRIO which are eligible for discounted pricing.

Government Rebates. The Company estimates a rebate liability in connection with a Medicaid Drug Rebate Agreement with the Centers for Medicare & Medicaid Services, which provides a rebate to participating states based on covered purchases of OTIPRIO. At the time of sale, the Company records estimated Medicaid rebates based on the Company's historical rebate activity, projected payer mix and Medicaid patient population industry data.

Distributor Fees. The Company's customers are specialty wholesale distributors with whom the Company has contracted to pay a fee for service based on a percentage of gross product sales. This fee for service is recorded as an allowance against accounts receivable at the time of sale based on the contracted percentage.

Concentration of Major Customers

The Company sells OTIPRIO to specialty wholesale distributor customers. The Company's sales to its three largest customers in 2017 accounted for approximately 34%, 34% and 30%, respectively, of the Company's 2017 annual revenues. The Company's sales to its three largest customers in 2016 accounted for approximately 35%, 34% and 30%, respectively, of the Company's 2016 annual revenues.

Research and Development

Research and development expenses include the costs associated with the Company's research and development activities, including salaries, benefits and occupancy costs. Also included in research and development expenses are third-party costs incurred in conjunction with contract manufacturing for the Company's research and

development programs and clinical trials, including the cost of clinical trial drug supply, costs incurred by contract research organizations and regulatory expenses. Research and development costs are expensed as incurred.

Patent Expenses

The Company expenses all costs as incurred in connection with patent applications (including direct application fees, and the legal and consulting expenses related to making such applications) and such costs are included in selling, general and administrative expenses in the statements of operations.

Stock-Based Compensation

The Company accounts for stock-based compensation expense related to stock options and employee stock purchase plan (ESPP) rights by estimating the fair value on the date of grant using the Black-Scholes-Merton option pricing model. For awards subject to time-based vesting conditions, stock-based compensation expense is recognized using the straight-line method. The Company early adopted ASU 2016-09 as of January 1, 2016 and made a policy election to account for forfeitures as they occur. The cumulative effect of adoption was immaterial.

Income Taxes

The accounting guidance for uncertainty in income taxes prescribes a recognition threshold and measurement attribute criteria for the financial statement recognition and measurement of tax positions taken or expected to be taken in a tax return. For those benefits to be recognized, a tax position must be more likely than not to be sustained upon examination by taxing authorities based on the technical merits of the position.

The Company uses the liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial reporting and the tax reporting basis of assets and liabilities and are measured using the enacted tax rates and laws that are expected to be in effect when the differences are expected to reverse. The Company provides a valuation allowance against net deferred tax assets unless, based upon the available evidence, it is more likely than not that the deferred tax assets will be realized. When the Company establishes or reduces the valuation allowance against its deferred tax assets, its provision for income taxes will increase or decrease, respectively, in the period such determination is made.

Comprehensive Loss

Comprehensive loss is defined as the change in equity during a period from transactions and other events and/or circumstances from non-owner sources.

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, potentially dilutive securities are excluded from the calculation of diluted net loss per share because their effect would be anti-dilutive and therefore, basic and diluted net loss per share were the same for all periods presented.

Potentially dilutive securities excluded from the calculation of diluted net loss per share are as follows:

	Years Ended December 31,		
	2017	2016	2015
Warrants to purchase common stock	—	141,060	141,060
Unvested restricted common stock subject to repurchase	—	—	2,964
Options to purchase common stock	4,599,252	5,149,973	3,413,142
Total	4,599,252	5,291,033	3,557,166

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update No. 2014-09, “Revenue from Contracts with Customers” (ASU 2014-09). ASU 2014-09 supersedes nearly all existing revenue recognition guidance under U.S. GAAP and requires revenue to be recognized when promised goods or services are transferred to customers in an amount that reflects the consideration that is expected to be received for those goods or services. Additionally, qualitative and quantitative disclosures are required about customer contracts, significant judgments and changes in judgments, and assets recognized from the costs to obtain or fulfill a contract. The FASB has also recently issued several amendments to ASU 2014-09, including clarification on accounting for licenses of intellectual property and identifying performance obligations.

ASU 2014-09 is effective for the Company beginning in the first quarter of 2018 using one of two prescribed transition methods: retrospectively to each prior reporting period presented (full retrospective method), or retrospectively with the cumulative effect of initially applying the guidance recognized at the date of initial application (the cumulative catch-up transition method). The Company will adopt ASU 2014-09 in the first quarter of 2018 using the full retrospective method to restate each prior reporting period presented.

The Company has evaluated the effect that updated standard and transition method will have on its internal processes, financial statements and related disclosures. The Company has used internal resources and third-party service providers to assist in the evaluation. While the Company continues to assess all potential impacts under ASU 2014-09, recognition of the Company’s revenue under the new standard is expected to be materially consistent with the Company’s current revenue recognition policy. The new standard is not expected to materially impact the timing or amounts of revenue recognized.

In January 2016, the FASB issued ASU No. 2016-01, “Financial Instruments – Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities” (ASU 2016-01). ASU 2016-01 requires equity investments (except those accounted for under the equity method of accounting, or those that result in consolidation of the investee) to be measured at fair value with changes in fair value recognized in net income. ASU 2016-01 requires public business entities to use the exit price notion when measuring the fair value of financial instruments for disclosure purposes, requires separate presentation of financial assets and financial liabilities by measurement category and form of financial asset, and eliminates the requirement for public business entities to disclose the method(s) and significant assumptions used to estimate the fair value that is required to be disclosed for financial instruments measured at amortized cost. These changes become effective for the Company's fiscal year beginning January 1, 2018. The Company is currently evaluating the effect ASU 2016-01 will have on its financial statements and related disclosures and does not anticipate that the adoption of this standard will have a material impact on its

financial statements.

In February 2016, the FASB issued ASU No. 2016-02, "Leases" (ASU 2016-02). ASU 2016-02 provides accounting guidance for both lessee and lessor accounting models. Among other things, lessees will recognize a right-of-use asset and a lease liability for leases with a duration of greater than one year. For statement of operations purposes, ASU 2016-02 will require leases to be classified as either operating or finance. Operating leases will result in straight-line expense while finance leases will result in a front-loaded expense pattern. The new standard will be effective for the Company on January 1, 2019 and will be adopted using a modified retrospective approach which will require application of the new guidance at the beginning of the earliest comparative period presented. The

Company is currently evaluating the effect that ASU 2016-02 will have on its financial statements and related disclosures.

In August 2016, the FASB issued ASU 2016-15, “Statement of Cash Flows (Topic 230) Classification of Certain Cash Receipts and Cash Payments” (ASU 2016-15), which applies to all entities that are required to present a statement of cash flows under Topic 230. ASU 2016-15 addresses the presentation and classification of cash flows related to (i) debt prepayment or debt extinguishment costs, (ii) settlement of zero-coupon debt instruments or other debt instruments with coupon interest rates that are insignificant in relation to the effective interest rate of the borrowing, (iii) contingent consideration payments made after a business combination, (iv) proceeds from the settlement of insurance claims, (v) proceeds from the settlement of corporate-owned life insurance policies (including bank-owned life insurance policies), (vi) distributions received from equity method investees, (vii) beneficial interests in securitization transactions, and (viii) separately identifiable cash flows and application of the predominance principle. The amendments in ASU 2016-15 should be applied using a retrospective transition method to each period presented, unless it is impracticable. The Company does not expect the adoption of ASU 2016-15, which will be effective for it beginning January 1 2018, to have a material impact on its statement of cash flows.

In May 2017, the FASB issued Accounting Standards Update No. 2017-09, “Compensation - Stock Compensation (Topic 718)” (ASU 2017-09). ASU 2017-09 provides clarification on when modification accounting should be used for changes to the terms or conditions of a share-based payment award. ASU 2017-09 does not change the accounting for modifications but clarifies that modification accounting guidance should only be applied if there is a change to the value, vesting conditions or award classification and would not be required if the changes are considered non-substantive. The new standard is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2017. Early adoption is permitted. The Company is currently evaluating the effect ASU 2017-09 will have on its financial statements and related disclosures and does not anticipate that the adoption of this standard will have a material impact on its financial statements.

3. Available-for-Sale Securities

The Company invests in available-for-sale securities consisting of money market funds, certificates of deposit, U.S. treasury securities and U.S. government sponsored enterprise securities. Available-for-sale securities are classified as part of either cash and cash equivalents or short-term investments in the balance sheets. Available-for-sale securities with maturities of three months or less from the date of purchase have been classified as cash equivalents, and were $10.5 million and $18.5 million as of December 31, 2017 and 2016, respectively. Available-for-sale securities with maturities of more than three months from the date of purchase have been classified as short-term investments, and were as follows as of (in thousands):

	Amortized Cost	Unrealized Gain	Unrealized Loss	Market Value
December 31, 2017:				
U.S. treasury securities	$ 39,209	$ —	$ (44)	$ 39,165
U.S. government sponsored enterprise securities	62,439	—	(56)	62,383
Total available-for-sale securities	$ 101,648	$ —	$ (100)	$ 101,548
December 31, 2016:				
U.S. treasury securities	$ 45,625	$ —	$ (26)	$ 45,599
U.S. government sponsored enterprise	121,694	4	(19)	121,679

securities				
Certificates of deposit	4,944	—	—	4,944
Total available-for-sale securities	$ 172,263	$ 4	$ (45)	$ 172,222

As of December 31, 2017, the Company had 35 securities in a gross unrealized loss position, all of which have been in such position for less than twelve months. At each reporting date, the Company performs an evaluation of impairment to determine if the unrealized losses are other-than-temporary. Factors considered in determining whether a loss is other-than-temporary include the length of time and extent to which fair value has been less than the cost basis, the financial condition of the issuer, and the Company's intent and ability to hold the investment until

recovery of its amortized cost basis. Management intends, and have the ability, to hold its investments in unrealized loss positions until their amortized cost basis has been recovered. The Company determined that there were no other-than-temporary declines in the value of any available-for-sale securities as of December 31, 2017. All the Company's available-for-sale investment securities mature within one year.

The Company obtains the fair value of its available-for-sale securities from a professional pricing service. The fair values of available-for-sale securities are validated by comparing the fair values reported by the professional pricing service to quoted market prices or to fair values obtained from the custodian bank.

4. Balance Sheet Details

Prepaid and Other Current Assets

Prepaid and other current assets are comprised of the following (in thousands):

	December 31,	
	2017	2016
Prepaid clinical trial costs	$729	$2,161
Other	1,599	2,155
Total	$2,328	$4,316

Inventory

Inventory is comprised of the following (in thousands):

	December 31,	
	2017	2016
Raw materials	$—	$214
Work in-process	—	916
Finished goods	6	305
Total	$6	$1,435

During the years ended December 31, 2017 and 2016, the Company recorded an inventory write down of $1.5 million and $0.3 million, respectively, for inventory nearing expiration and/or inventory in excess of current expected customer demand.

Property and Equipment, Net

Property and equipment, net consists of the following (in thousands):

	December 31,	
	2017	2016
Laboratory equipment	$3,457	$2,910
Manufacturing equipment	871	870
Computer equipment and software	731	733
Leasehold improvements	733	830
Office furniture	1,581	1,474
	7,373	6,817
Less: accumulated depreciation and amortization	(2,694)	(1,840)
Total	$4,679	$4,977

Depreciation expense was $1.3 million, $0.7 million and $0.4 million for the years ended December 31, 2017, 2016 and 2015, respectively.

Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31,	
	2017	2016
Accrued clinical trial costs	$1,112	$4,352
Accrued other	2,769	4,712
Total	$3,881	$9,064

5. Restructuring Charges

In November 2017, the Company initiated a restructuring plan to focus resources on its development programs and eliminate the cash burn associated with OTIPRIO promotional support. OTIPRIO continues to be available for purchase by customers while the Company evaluates commercial partnering options for the product, including divestiture. The actions associated with the restructuring were substantially completed in December 2017 and, as a result the Company recorded a one-time restructuring charge of $3.8 million to selling, general and administrative expense. Restructuring costs primarily include severance costs, including severance payments and outplacement services, health insurance coverage and $1.0 million in stock-based compensation expense associated with accelerated vesting pursuant to the original terms of the Company’s employment agreement with its Chief Medical Officer. As of December 31, 2017, accrued and unpaid severance costs totaled approximately $1.5 million.

6. Commitments and Contingencies

Operating Leases

In December 2016, the Company moved into its new headquarters location in San Diego, California. The lease commenced in December 2016 and has an initial term of 130 months, with an option by the Company to extend the lease term for an additional five years. The Company has the right to terminate the lease at the end of the 94th month of the lease term if it is acquired by a third party and pays an early termination fee. The Company is responsible for payment of taxes and operating expenses for the building, in addition to monthly base rent in the initial amount of approximately $232,000, with 3% annual increases, which monthly base rent is abated for the first ten months of the lease term. The total estimated base rent payments over the life of the lease are estimated to be approximately $32.7 million. Upon execution of the lease in May 2015, the Company provided a security deposit in the form of a letter of credit in the amount of approximately $695,000. Cash collateralizing the letter of credit is classified as noncurrent restricted cash on the balance sheets. The Company has determined that the lease is an operating lease for accounting purposes.

Rent expense was $3.2 million, $1.1 million and $0.7 million for the years ended December 31, 2017, 2016 and 2015, respectively. For financial reporting purposes, rent expense is recognized on a straight-line basis over the term of the lease. Accordingly, rent expense recognized in excess of rent paid is accounted for as deferred rent in the balance sheets.

As of December 31, 2017, future minimum annual obligations under all non-cancellable operating lease commitments, including the facility leases described above are as follows (in thousands):

2018	$3,034
2019	3,003
2020	3,084
2021	3,136
2022	3,229
Thereafter	16,718
Total	$32,204

Litigation

From time to time, the Company may be involved in various lawsuits, legal proceedings, or claims that arise in the ordinary course of business. Management believes there are no claims or actions pending against the Company as of December 31, 2017 which will have, individually or in the aggregate, a material adverse effect on its business, liquidity, financial position, or results of operations. Litigation, however, is subject to inherent uncertainties, and an adverse result in these or other matters may arise from time to time that may harm the Company's business.

Intellectual Property Licenses

The Company has acquired exclusive rights to develop patented rights, information rights and related know-how for OTIPRIO, certain of its product candidates and potential future product candidates under licensing agreements with third parties. The licensing rights obligate the Company to make payments to the licensors for license fees, milestones and royalties. The Company is also responsible for patent prosecution costs, in the event such costs are incurred.

Under one of these agreements, the Company has achieved six development milestones and one regulatory milestone, totaling $2.8 million, related to its clinical trials for OTIPRIO, OTIVIDEX and OTO-311. The Company may be obligated to make additional milestone payments under the Company's intellectual property license agreements as follows (in thousands):

Development	$1,600
Regulatory	10,275
Commercialization	1,000
Total	$12,875

In addition, the Company is obligated to pay royalties of less than five percent on net sales of OTIPRIO and on sales of any other commercial products developed using these licensed technologies. Such royalty expense for OTIPRIO is recorded to cost of product sales. The Company may also be obligated to pay the licensors a percentage of fees received if and when the Company sublicenses the technology. As of December 31, 2017, the Company has not entered into any sublicense agreements for the licensed technologies.

The following table summarizes costs recognized, in research and development, under the Company's license agreements and other non-cancellable royalty and milestone obligations (in thousands):

	Years Ended December 31,		
	2017	2016	2015
License and other fees	$—	$ 71	$622
Milestone fees	—	—	1,600
Total license and related fees	$—	$ 71	$2,222

Other Royalty Arrangements

The Company entered into an agreement related to OTIPRIO under which the Company is obligated to pay a one-time milestone payment of $0.5 million upon the first commercial sale of OTIPRIO and to pay royalties of less than one percent on net product sales of OTIPRIO. This milestone payment was paid during March 2016 and both this milestone payment and the royalties are recorded as selling, general and administrative expense. The royalties are payable until the later of: (i) the expiration of the last to expire patent owned by the Company in such country covering OTIPRIO; or (ii) 10 years after the first commercial sale of OTIPRIO after receipt of regulatory approval for OTIPRIO in such country.

The Company entered an exclusive license agreement with Ipsen that enables the Company to use clinical and nonclinical gacyclidine data generated by Ipsen to support worldwide development and regulatory filings for OTO-313. Under this license agreement, the Company is obligated to pay Ipsen low single-digit royalties on annual net

sales of OTO-313 by the Company or its affiliates or sublicensees, up to a maximum cumulative royalty totaling $10.0 million.

7. Fair Value

The accounting guidance defines fair value, establishes a consistency framework for measuring fair value and expands disclosure for each major asset and liability category measured at fair value on either a recurring basis or nonrecurring basis. Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants on the measurement date. Accounting guidance establishes a three-tier fair value hierarchy that requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. These tiers are based on the source of the inputs and are as follows:

Level 1: Observable inputs such as quoted prices in active markets for identical assets or liabilities.

Level 2: Inputs other than quoted prices in active markets that are observable either directly or indirectly.

Level 3: Unobservable inputs in which there is little or no market data, which require the reporting entity to develop its own assumptions.

As of December 31, 2017 and 2016, the Company held no assets or liabilities measured at fair value on a nonrecurring basis and no liabilities measured at fair value on a recurring basis. The following fair value hierarchy table presents the Company’s assets measured at fair value on a recurring basis (in thousands):

	Fair Value Measurement at Reporting Date Using			
	Total	Level 1	Level 2	Level 3
December 31, 2017:				
Assets				
Money market funds	$10,494	$10,494	$—	$ —
U.S. treasury securities	39,165	39,165	—	—
U.S. government sponsored enterprise securities	62,383	—	62,383	—
Total	$112,042	$49,659	$62,383	$ —
December 31, 2016:				
Assets				
Money market funds	$18,476	$18,476	$—	$ —
U.S. treasury securities	45,599	45,599	—	—
U.S. government sponsored enterprise securities	121,679	—	121,679	—
Certificates of deposit	4,944	—	4,944	—
Total	$190,698	$64,075	$126,623	$ —

8. Stockholders’ Equity

Common Stock Reserved for Future Issuance

Shares of common stock reserved for future issuance are as follows:

	December 31,	
	2017	2016
Warrants for the purchase of common stock	—	141,060
Common stock options issued and outstanding	4,599,252	5,149,973
Common stock options available for future grant	3,403,597	1,531,216
Common stock reserved for issuance under ESPP	1,292,327	918,569
Total common stock reserved for future issuance	9,295,176	7,740,818

During 2017, 141,060 warrants were net exercised for 32,209 shares of common stock. There are no remaining warrants outstanding at December 31, 2017.

9. Stock-Based Compensation and Equity Plans

2014 Equity Incentive Plan

The Company granted awards under its 2010 Equity Incentive Plan (the 2010 Plan) until June 2014. In July 2014, the Company's board of directors adopted and the Company's stockholders approved its 2014 Equity Incentive Plan (the 2014 Plan), which became effective in August 2014. In connection with the adoption of the 2014 Plan, the Company terminated the 2010 Plan for future use and provided that no further equity awards were to be granted under the 2010 Plan. All outstanding awards under the 2010 Plan continue to be governed by their existing terms.

The 2014 Plan permits the grant of incentive stock options to the Company's employees and the grant of nonstatutory stock options, restricted stock, restricted stock units, stock appreciation rights, performance units and performance shares to the Company's employees, directors and consultants. Options granted under the 2014 Plan generally vest over four years, subject to continued service, and subject to certain acceleration of vesting provisions, expire no later than 10 years from the date of grant. Options granted under the 2014 Plan must have a per share exercise price equal to at least 100% of the fair market value of a shares of the common stock as of the date of grant.

Under the evergreen provision of the 2014 Plan, the number of shares available for issuance under the 2014 Plan includes an annual increase on the first day of each fiscal year equal to the lesser of (i) 2,500,000 shares; (ii) 5% of the outstanding shares of common stock as of the last day of the immediately preceding fiscal year; or (iii) such other amount as the Company's board of directors may determine. Effective January 1, 2018, the number of shares available for future issuance was increased by 1,527,936 shares so that the total available for future issuance as of January 1, 2018 will be 4,931,533 shares.

As of December 31, 2017, 3,403,597 options were available for grant under the 2014 Plan. The following table summarizes stock option activity for the year ended December 31, 2017 (in thousands except per share amounts and years):

	Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (In Years)	Aggregate Intrinsic Value
Outstanding as of December 31, 2016	5,150	$ 15.01		
Granted	1,540	$ 14.47		
Exercised	(191)	$ 2.34		
Forfeited	(1,900)	$ 17.62		
Outstanding as of December 31, 2017	4,599	$ 14.28	6.9	$ 3,577

Options vested and expected to vest as of December 31, 2017	4,599	$ 14.28	6.9	$ 3,577
Options exercisable as of December 31, 2017	2,792	$ 12.74	5.7	$ 3,556

The following table summarizes certain information regarding stock options (in thousands, except per share data):

	Years Ended December 31,		
	2017	2016	2015
Weighted-average grant date fair value per share of options granted during the period	$9.14	$9.47	$18.16
Cash received from options exercised during the period	448	355	646
Intrinsic value of options exercised during the period	623	985	4,036

2014 Employee Stock Purchase Plan

In July 2014, the Company's board of directors adopted and the stockholders approved the Company's 2014 Employee Stock Purchase Plan (the ESPP), which became effective upon adoption by the Company's board of directors. The ESPP allows eligible employees to purchase shares of the Company's common stock at a discount through payroll deductions of up to 15% of their eligible compensation, subject to any plan limitations. The offering periods generally start on the first trading day on or after June 1 and December 1 of each year and ends on the first trading day on or before June 1 and December 1 approximately twenty-four months later, and include six-month purchase periods.

The number of shares available for issuance under the ESPP includes an annual increase on the first day of each fiscal year, equal to the lesser of (i) 800,000 shares; (ii) 1.5% of the outstanding shares of common stock as of the last day of the immediately preceding fiscal year; or (iii) such other amount as the Company's board of directors may determine. Effective January 1, 2018, the number of shares available for future issuance was increased by 458,380 shares so that the total available for future issuance as of January 1, 2018 will be 1,750,707 shares.

As of December 31, 2017, the Company had issued 224,058 shares of common stock under the ESPP and had 1,292,327 shares available for future issuance.

Stock-Based Compensation Expense

The following are the weighted-average underlying assumptions used to determine the fair value of stock options and ESPP rights using the Black-Scholes-Merton option pricing model:

	Years Ended December 31,		
	2017	2016	2015
Stock Options:			
Risk-free interest rate	2.1%	1.5%	1.7%
Expected dividend yield	0.0%	0.0%	0.0%
Expected volatility	69.8%	67.8%	76.6%
Expected term (in years)	6.1	6.1	6.1
Employee Stock Purchase Plan:			
Risk-free interest rate	1.4%	0.8%	0.5%
Expected dividend yield	0.0%	0.0%	0.0%
Expected volatility	106.6%	70.8%	70.8%
Expected term (in years)	1.2	1.3	1.3

Risk-Free Interest Rate. The Company bases the risk-free interest rate assumption on observed interest rates appropriate for the expected term of the option grants.

Expected Dividend Yield. The Company bases the expected dividend yield assumption on the fact that it has never paid cash dividends and has no present intention to pay cash dividends.

Expected Volatility. The expected volatility assumption is based on volatilities of a peer group of similar companies whose share prices are publicly available. The peer group was developed based on companies in the biopharmaceutical industry.

Expected Term. The expected term represents the period of time that options are expected to be outstanding. Because the Company does not have historical exercise behavior, it determines the expected life assumption using the simplified method, which is an average of the contractual term of the option and its ordinary vesting period.

Total non-cash stock-based compensation expense recognized in the statements of operations is as follows (in thousands):

	Years Ended December 31,		
	2017	2016	2015
Cost of product sales	$20	$41	$—
Research and development	3,763	2,996	2,969
Selling, general and administrative	9,878	9,574	4,747
Total stock-based compensation	$13,661	$12,611	$7,716

As of December 31, 2017, unrecognized compensation costs related to stock options was $14.5 million which is expected to be recognized over a remaining weighted-average vesting period of 2.2 years. As of December 31, 2017, unrecognized compensation cost related to ESPP rights was $0.8 million which is expected to be recognized over a remaining weighted-average vesting period of 1.2 years.

10. Income Taxes

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 that a cumulative change in ownership of more than 50% occurs within a three-year period. The Company has completed an IRC Section 382/383 analysis, regarding the limitation of net operating loss and research and development credit carryforwards as of December 31, 2017. As a result of the analysis, three ownership changes were determined to have occurred. Based on these changes, the deferred tax assets for net operating losses and federal research and development credits of $2.2 million and $0.3 million, respectively, have been removed from the deferred tax asset schedule and the Company has recorded a corresponding decrease in the valuation allowance. The California research and development credits were not limited as these credits carry forward indefinitely. The Company will continue to consider changes in ownership that may cause losses of tax attributes in the future.

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

	December 31,	
	2017	2016
Deferred tax assets:		
Net operating loss carryforwards	$53,666	$64,246
Research and development credits	6,603	5,263
Depreciation and amortization	15,916	21,631
Accrued expenses	394	1,619
Deferred rent	636	238
Stock compensation	5,610	6,437
Other, net	451	133
Total deferred tax assets	83,276	99,567
Less: valuation allowance	(83,276)	(99,567)
Total	$—	$—

Due to the Company’s history of losses and uncertainty regarding future earnings, a full valuation allowance has been recorded against the Company’s deferred tax assets, as it is more likely than not that such assets will not be realized. A valuation allowance of approximately $83.3 million and $99.6 million has been established as of December 31, 2017 and 2016, respectively.

The Company elected to early adopt ASU 2016-09 as of January 1, 2016. As a result of the adoption, the balance of the Company’s unrecognized excess tax benefits of $1.1 million was reversed as of December 31, 2016 with the impact recorded to retained earnings. Due to the full valuation allowance on the Company's deferred tax assets, there was no impact to the financial statements.

At December 31, 2017, the Company had federal and state net operating loss carryforwards of approximately $241.6 million and $101.3 million, respectively, net of IRC Section 382 limitations. The federal and state net operating loss carryforwards will begin to expire in 2030, unless previously utilized. At December 31, 2017, the Company also had federal and California research and development credit carryforwards of approximately $7.9 million net of IRC Section 383 limitations and $3.9 million, respectively. The federal research and development credit carryforwards will begin expiring in 2030 unless previously utilized. The California research credit will carry forward indefinitely.

The following is a reconciliation of the expected recovery of income taxes between those that are based on enacted tax rates and laws, to those currently reported for the years ended December 31 (in thousands):

	2017	2016	2015
Federal statutory rate	$(30,645)	$(37,599)	$(20,967)
State tax (net of federal benefit)	(462)	(2,079)	2
Permanent items, other	1,376	164	11
Stock compensation	1,720	609	292
Other adjustments	—	—	(847)
Rate change	45,421	(2,251)	1,637
Research and development credits	(1,830)	(3,210)	(1,672)
Uncertain tax positions	732	2,124	2,865
Change in valuation allowance	(16,312)	42,243	18,680
Provision for income taxes	$0	$1	$1

The Tax Cuts and Jobs Act (the Act) was enacted on December 22, 2017. The Act amends the Internal Revenue Code to reduce tax rates and modify policies, credits, and deductions for individuals and business. For businesses, the Act reduces the corporate tax rate from a maximum of 35% to a flat 21% rate. The rate reduction is effective on January 1, 2018. At December 31, 2017, the Company has not completed its accounting for the tax effects of enactment of the Act; however, in certain cases, as described below, we have made a reasonable estimate of the effects on our existing tax balances. The Company will continue to make and refine its calculations as additional analysis is completed. In addition, the Company’s estimates may also be affected as it gains a more thorough understanding of the tax law.

The Company remeasured certain deferred tax assets based on the rates at which they are expected to reverse in the future, which is generally 21%. As a result, the Company has reduced its deferred tax asset balance as of December 31, 2017 by $44.5 million. Due to the Company’s full valuation allowance position, the Company has also reduced the valuation allowance by the same amount. The Company is still analyzing certain aspects of the Act and refining our calculations, which could potentially affect the measurement of these balances or potentially give rise to new deferred tax amounts.

Due to the uncertainties which currently exist in the interpretation of the provisions of the Act regarding Internal Revenue Code Section 162(m), the Company has not evaluated the potential impact of IRC Section 162(m) as amended by the Act on its financial statements. However, we are still analyzing certain aspects of the Act and refining our calculations, which could potentially affect the measurement of these balances or potentially give rise to new deferred tax assets.

On December 22, 2017, Staff Accounting Bulletin No. 118 (SAB 118) was issued to address the application of US GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of the Act. In accordance, with SAB 118, the Company has determined that there is no deferred tax benefit or expense with respect to the remeasurement of certain deferred tax assets and liabilities due to the full valuation allowance against net deferred tax assets. Additional analysis, of the law and the impact to the Company will be performed and any impact will be recorded in the respective quarter in 2018.

The following table summarizes the activity related to our gross unrecognized tax benefits (in thousands):

	December 31,		
	2017	2016	2015
Balance at the beginning of the year	$8,391	$5,709	$1,774
Adjustments related to prior year tax positions	—	1,872	3,188
Increases related to current year tax positions	798	1,409	747
Decreases for tax positions from prior years	(91)	(599)	—
Decreases due to statute of limitations expiration	—	—	—
Decreases due to IRC Section 382/383 limitation	—	—	—
	$9,098	$8,391	$5,709

The Company's policy is to include interest and penalties related to unrecognized income tax benefits as a component of income tax expense. The Company has no accruals for interest or penalties in the balance sheets as of December 31, 2017 and 2016 and has not recognized interest or penalties in the statements of operations for the years ended December 31, 2017, 2016 and 2015.

Due to the valuation allowance recorded against the Company's deferred tax assets, future changes in unrecognized tax benefits will not impact the Company's effective tax rate. The Company does not expect its unrecognized tax benefits to change significantly in the next 12 months.

The Company is subject to taxation in the United States for federal and state purposes. Due to the net operating loss carryforwards, the U.S. federal and state returns are open to examination by the IRS and state tax authorities for all years since inception. The Company is not currently under examination by the federal or any state tax authority.

11. Selected Quarterly Financial Data (unaudited)

The following table contains quarterly financial information for 2017 and 2016. The Company believes that the following information reflects all normal recurring adjustments necessary for a fair statement of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
	(in thousands, except per share data)			
Year Ended December 31, 2017				
Product sales, net	$358	$ 326	$ 282	$ 270
Total costs and operating expenses	27,740	23,858	21,599	19,440
Other income	304	311	319	337
Net loss	(27,078)	(23,221)	(20,998)	(18,833)
Net loss per share, basic and diluted	(0.89)	(0.77)	(0.69)	(0.62)
Year Ended December 31, 2016				
Product sales, net	$13	$ 76	$ 321	$ 273
Total costs and operating expenses	26,876	29,983	28,179	27,126

Other income	100	231	286	281
Net loss	(26,763)	(29,676)	(27,572)	(26,572)
Net loss per share, basic and diluted	(0.91)	(0.98)	(0.91)	(0.88)

Item 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

Item 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Management, with the participation of our Chief Executive Officer and our Chief Financial and Business Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2017. 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 the evaluation of our disclosure controls and procedures as of December 31, 2017, our Chief Executive Officer and our Chief Financial and Business Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act). Our management conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria established in "Internal Control - Integrated Framework" (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on the assessment, management has concluded that our internal control over financial reporting was effective as of December 31, 2017. This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm on our internal control over financial reporting due to an exemption established by the JOBS Act for "emerging growth companies."

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during the quarter ended December 31, 2017 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations of Disclosure Controls and Internal Control over Financial Reporting

Because of their inherent limitations, our disclosure controls and procedures and our internal control over financial reporting may not prevent material errors or fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. The effectiveness of our disclosure controls and procedures and our internal control over financial reporting is subject to risks, including

that the controls may become inadequate because of changes in conditions or that the degree of compliance with our policies or procedures may deteriorate.

Item 9B. OTHER INFORMATION

None.

Part III

Item 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this item will be contained in our definitive proxy statement to be filed with the Securities and Exchange Commission in connection with our 2018 annual meeting of stockholders (the "Proxy Statement"), which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2017, and is incorporated in this report by reference.

Item 11. EXECUTIVE COMPENSATION

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

Item 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

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

Item 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

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

Item 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

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

PART IV

Item 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

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

(1) Financial Statements:

Our Financial Statements are listed in the “Index to Financial Statements” under Part II, Item 8 of this Annual Report on Form 10-K.

(2) Financial Statement Schedules:

Schedules not listed above have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or notes herein.

(3) Exhibits:

The following exhibits, as required by item 601 of Regulation SK are attached or incorporated by reference as stated below

EXHIBIT INDEX

Exhibit Number	Description	Incorporation by Reference			
		Form	File No.	Exhibit	Filing Date
2.1#	Asset Transfer Agreement between the Registrant and IncuMed, LLC, dated April 30, 2013.	S-1	333-197365	2.1	7/11/2014
3.1	Amended and Restated Certificate of Incorporation of the Registrant.	S-1	333-197365	3.2	8/1/2014
3.2	Amended and Restated Bylaws of the Registrant.	S-1	333-197365	3.4	8/1/2014
4.1	Third Amended and Restated Investors' Rights Agreement among the Registrant and certain of its stockholders, dated April 23, 2014.	S-1	333-197365	4.1	7/11/2014
4.2	Specimen common stock certificate of the Registrant.	S-1	333-197365	4.2	7/28/2014
10.1+	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers.	S-1	333-197365	10.1	8/1/2014
10.2+	Amended and Restated 2010 Equity Incentive Plan and forms of agreement thereunder.	S-1	333-197365	10.2	8/1/2014
10.3+	2014 Equity Incentive Plan and forms of agreements thereunder.	S-1	333-197365	10.3	8/1/2014
10.4+	2014 Employee Stock Purchase Plan and form of agreement thereunder.	S-1	333-197365	10.4	8/1/2014
10.5+	Executive Incentive Compensation Plan.	S-1	333-197365	10.5	7/28/2014
10.6+	Executive Employment Agreement between the Registrant and David A. Weber, Ph.D., dated July 30, 2014.	S-1	333-197365	10.6	8/1/2014
10.7+	Executive Employment Agreement between the Registrant and Paul E. Cayer, dated July 31, 2014.	S-1	333-197365	10.7	8/1/2014
10.8+	Executive Employment Agreement between the Registrant and Robert Michael Savel, II, dated July 31, 2014.	S-1	333-197365	10.9	8/1/2014
10.9+	Executive Employment Agreement between the Registrant and Kathie Bishop, Ph.D., dated January 4, 2017.	10-Q	001-36591	10.1	5/4/2017

10.10	Loan and Security Agreement between the Registrant and Square 1 Bank, dated July 31, 2013.	S-1	333-197365	10.10	7/11/2014
10.11#	License and Commercialization Agreement between the Registrant and DURECT Corporation, dated April 30, 2013.	S-1	333-197365	10.11	7/11/2014
10.12#	License Agreement between the Registrant and The Regents of the University of California, dated November 5, 2008, as amended on January 27, 2010, June 9, 2010 and November 7, 2012.	S-1	333-197365	10.12	7/11/2014
10.13	Form of Warrant to Purchase Series A Convertible Preferred Stock issued pursuant to the Registrant's Note and Warrant Purchase Agreement, dated December 8, 2008.	S-1	333-197365	10.13	7/11/2014
10.14	Form of Warrant to Purchase Shares of Preferred Stock issued pursuant to the Registrant's Note and Warrant Purchase Agreement, dated August 23, 2012.	S-1	333-197365	10.14	7/11/2014
10.15	Warrant to Purchase Stock issued pursuant to Loan and Security Agreement between the Registrant and Square 1 Bank, dated July 31, 2013.	S-1	333-197365	10.15	7/11/2014

Exhibit Number	Description	Incorporation by Reference			
		Form	File No.	Exhibit	Filing Date
10.16+	Executive Employment Agreement between the Registrant and Dean Hakanson, M.D., dated March 17, 2015.	10-Q	001-36591	10.1	5/12/2015
10.17	Lease Agreement between the Registrant and ARE-SD Region No. 34, LLC, dated May 11, 2015.	10-Q	001-36591	10.2	5/12/2015
10.18+	Executive Employment Agreement between the Registrant and Eric Loumeau, dated May 15, 2015.	10-Q	001-36591	10.1	8/12/2015
23.1	Consent of Independent Registered Public Accounting Firm.				
31.1	Certification of Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act				
31.2	Certification of Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act				
32.1*	Certification of Chief Executive Officer pursuant to Section 906 of the Sarbanes-Oxley Act				
32.2*	Certification of Chief Financial Officer pursuant to Section 906 of the Sarbanes-Oxley Act				
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.				

* The certifications attached as Exhibit 32.1 and 32.2 that accompany this Annual Report on Form 10-K are not deemed filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of Otonomy, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report on Form 10-K, irrespective of any general incorporation language contained in such filing.

Portions of the exhibit have been omitted pursuant to an order granted by the Securities and Exchange Commission for confidential treatment.

+ Indicates management contract or compensatory plan.

Item 16. FORM 10-K SUMMARY

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this annual report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: March 8, 2018

OTONOMY, INC.

By: /s/ David A. Weber
David A. Weber, Ph.D.
President and Chief Executive Officer

POWER OF ATTORNEY

Each person whose signature appears below constitutes and appoints David A. Weber, Ph.D. and Paul E. Cayer, and each of them acting individually, as his or her true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them, or their or his substitutes, may lawfully do or cause to be done by virtue thereof.

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

Signature	Title	Date
/s/ David A. Weber	President, Chief Executive Officer and Director	March 8, 2018
David A. Weber, Ph.D.	(Principal Executive Officer)	
/s/ Paul E. Cayer	Chief Financial and Business Officer	March 8, 2018
Paul E. Cayer	(Principal Accounting Officer)	
/s/ Jay Lichter	Chairman of the Board of Directors	March 8, 2018
Jay Lichter, Ph.D.		
/s/ Vickie Capps	Director	March 8, 2018
Vickie Capps		

/s/ Iain McGill	Director	March 8, 2018
Iain McGill		
/s/ George J. Morrow	Director	March 8, 2018
George J. Morrow		
/s/ Heather Preston	Director	March 8, 2018
Heather Preston, M.D.		
/s/ Theodore R. Schroeder	Director	March 8, 2018
Theodore R. Schroeder		