Otonomy, Inc.
Form 10-K
March 18, 2015
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

x **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2014

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.)

6275 Nancy Ridge Drive, Suite 100

San Diego, California 92121

(Address of principal executive offices and Zip Code)

(858) 242-5200

(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
Class A 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

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

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 x

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 x 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 x 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. x

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

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

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

The aggregate market value of the common stock held by non-affiliates of the Company as of August 13, 2014 was approximately $149.4 million, based upon the closing price on The NASDAQ Global Select Market reported for such date. Shares of the registrant s common stock held by each executive officer, director and holder of 5% 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. The Company has elected to use August 13, 2014 as the calculation date, as on June 30, 2014 (the last business day of the Company s most recently completed second fiscal quarter) there was no public market for the Company s common stock.

As of March 9, 2015 the number of outstanding shares of the registrant s common stock, par value $0.001 per share, was 24,127,477.

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 2015 Annual Meeting of

Stockholders, which is expected to be filed not later than 120 days after the Registrant s fiscal year ended December 31, 2014.

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OTONOMY, INC.

ANNUAL REPORT ON FORM 10-K

FOR THE YEAR ENDED DECEMBER 31, 2014

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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, 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 our clinical development of OTO-104, including our expectations regarding the timing of results from our Phase 2b clinical trial and our plans regarding the initiation of a second pivotal trial;
- our expectations regarding the development of OTO-311;
- our expectations regarding our future development of our product candidates for additional indications;
- the timing or likelihood of regulatory filings and approvals, including our submission of an IND for OTO-311 with the FDA;
- our expectations regarding the future development of other product candidates;
- our expectations regarding our OTO-104 Phase 2b clinical trial potentially serving as one of two pivotal trials required to support U.S. regulatory approval;
- our expectations regarding the multiple-dose clinical safety requirement for U.S. regulatory approval of OTO-104 in the United States in patients with Ménière s disease;
- the potential for commercialization of our product candidates, if approved, including our expectations regarding the timing of the anticipated commercial launch for AuriPro in the United States, if approved;
- our expectations and statements regarding the potential pricing, market size, opportunity and growth potential for AuriPro and OTO-104, if approved for commercial use;

our expectations and statements regarding the adoption and use of AuriPro and OTO-104, if approved, by ENTs;

our expectations regarding potential coverage and reimbursement relating to AuriPro or OTO-104, 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 build 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 preclinical 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;

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developments and projections relating to our competitors and our industry;

our expectations regarding the expansion of our facilities; 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 those 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.

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PART I

Item 1. BUSINESS

Overview

We are a clinical-stage biopharmaceutical company focused on the development and commercialization of innovative therapeutics for the treatment of diseases and disorders of the ear. To overcome many of the limitations of delivering drugs to the middle and inner ear, we have developed a proprietary technology that is 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. Utilizing this technology, we have advanced three product candidates into development. Our lead product candidate, AuriPro, is a sustained-exposure antibiotic for which we have completed two identical Phase 3 clinical trials in 532 pediatric patients with middle ear effusion, or fluid, at the time of tympanostomy tube placement, or TTP, surgery. Results of these Phase 3 trials demonstrate that AuriPro achieved the primary efficacy endpoint with statistical significance ($p<0.001$) and that AuriPro was well tolerated. Based on these results, together with feedback received from a pre-NDA meeting and communications with the U.S. Food and Drug Administration, or FDA, and supportive results from the one year drug product stability testing required for filing, we submitted a New Drug Application, or NDA, for AuriPro to the FDA in February 2015. If approved within the standard review period, we anticipate a commercial launch for AuriPro in the United States in the first quarter of 2016. Our second product candidate, OTO-104, is a sustained-exposure steroid that is in a Phase 2b clinical trial for patients with Ménière s disease. We announced in December 2014 that we had achieved the target patient enrollment in this trial and expect to report results in the second quarter of 2015. During October 2014, we began enrollment in a multiple-dose safety study in Ménière s patients in the United Kingdom. Our third product candidate, OTO-311, is in preclinical development for the treatment for tinnitus. We plan to file an Investigational New Drug application, or IND, with the FDA for OTO-311 and initiate a Phase 1 clinical trial in 2015. There are no drugs approved by the FDA for the lead indications we are currently pursuing for our product candidates.

We estimate that more than 50 million people in the United States are affected by otic disorders and that approximately 20 million patients currently seek treatment each year for the most common conditions, including ear infections, balance disorders, tinnitus and hearing loss. As a result, we believe the existing market for treatments is significant and that there also remains a large population of untreated patients. Despite this large market opportunity, we believe the otic field has generally been overlooked by drug developers at least in part because of challenges in effectively delivering drug to the middle and inner ear. We believe that our sustained-exposure drug delivery technology overcomes some of these limitations, and that our product candidates address important unmet medical needs in the emerging otology market.

Our pipeline includes the following three product candidates:

AuriPro is a sustained-exposure formulation of the antibiotic ciprofloxacin in development for the treatment of middle ear effusion in pediatric patients requiring TTP surgery. We have completed two identical Phase 3 clinical trials that enrolled a total of 532 pediatric patients at approximately 60 centers in the United States and Canada. Results of these trials demonstrate that AuriPro achieved the primary efficacy endpoint, reduction in the incidence of treatment failures, with statistical significance ($p<0.001$) and that AuriPro was well tolerated. In these trials, AuriPro reduced the risk of treatment failure, as measured by the occurrence of post-operative otorrhea (drainage) or any use of rescue antibiotics, by an average of 49% in all randomized patients across the two trials, and the rate of

post-operative otorrhea or use of rescue antibiotics for documented otorrhea or otitis media by an average of 62% in all randomized patients across the two trials (p£0.004), in each case as compared to sham. Based on these results, together with feedback received from a pre-NDA meeting and communications with the FDA and supportive results from the one year stability testing required for filing, we submitted an NDA for AuriPro to the FDA in February 2015. If approved within the standard review period, we anticipate a commercial launch for AuriPro in the United States in the first quarter of 2016.

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OTO-104 is a sustained-exposure formulation of the steroid dexamethasone in development for the treatment of Ménière s disease and other inner ear conditions. We are conducting a Phase 2b clinical trial at more than 50 centers in the United States and Canada, which we believe will serve as one of two pivotal, single-dose efficacy trials required to support U.S. regulatory approval. In December 2014, we announced that we had achieved the target patient enrollment of 140 patients, and subsequently concluded enrollment with a total of 154 patients. We expect to report results from this clinical trial in the second quarter of 2015. If results are positive, we plan to initiate a second pivotal trial of OTO-104 in 2015. During October 2014, we began enrollment in a multiple-dose safety study in Ménière s patients in the United Kingdom. The prospective, randomized, placebo-controlled study, designed to evaluate the safety of multiple doses of OTO-104, will enroll 125 patients across multiple trial sites in the United Kingdom. In the first part of the study, patients will be randomized to receive two doses of either placebo or 12 mg OTO-104 by intratympanic (IT) injection given at three month intervals. Patients completing the double-blind portion of the study will be eligible to participate in an open-label extension study where all patients will receive two IT injections of OTO-104 at three month intervals. We intend to use data from this U.K. study together with one or more additional multiple-dose safety studies that we plan to initiate during 2015 to satisfy our multiple-dose clinical safety requirement for U.S. regulatory approval of OTO-104 in patients with Ménière s disease which we believe, based on discussions from an End-of-Phase 1 meeting with the FDA, will require 100 patients treated for one year and 300 patients treated for six months. The FDA has granted OTO-104 Fast Track designation.

OTO-311 is a sustained-exposure formulation of the N-Methyl-D-Aspartate, or NMDA, receptor antagonist gacyclidine in development for the treatment of tinnitus. We plan to file an IND with the FDA for OTO-311 and initiate a Phase 1 clinical trial in 2015. In November 2014, we announced the completion of an exclusive license agreement with Ipsen that enables us to use clinical and non-clinical gacyclidine data generated by Ipsen to support worldwide development and regulatory filings for OTO-311.

We have global commercialization rights to our product candidates. Our strategy is to advance our product candidates to regulatory approval and self-commercialize in the United States. In October 2014, we announced the appointment of an experienced Chief Commercial Officer to prepare for the commercialization of AuriPro, if approved. We plan to build a focused sales force targeting otolaryngologists, also known as ear, nose and throat physicians, or ENTs, who specialize in the treatment of patients affected by diseases and disorders of the ear. Outside the United States, we plan to evaluate whether to commercialize our products on our own or in collaboration with partners. We have a broad patent portfolio of approximately 60 issued patents and allowed patent applications and at least 85 pending patent applications covering our product candidates and indications as well as other potential applications of our technology in major markets around the world.

Our mission is to develop and commercialize novel and best-in-class therapeutics to address unmet medical needs in the emerging otology market. We were founded in 2008 by Jay Lichter, Ph.D., a partner at Avalon Ventures, together with Jeffrey Harris, M.D., Ph.D., Chief of the Division of Otolaryngology-Head and Neck Surgery at the University of California, San Diego, and several other experts in the field of otology. Dr. Lichter became interested in otology after suffering a severe attack of vertigo that was subsequently diagnosed by Dr. Harris as Ménière s disease. Dr. Lichter s battle with Ménière s disease, and his first-hand experience with the limitations of available treatments, led to the founding of Otonomy.

In order to execute our mission, we have assembled an experienced management team backed by a strong group of institutional healthcare investors. Our management team has extensive drug development and commercialization

capabilities led by David A. Weber, Ph.D., our President and Chief Executive Officer. Dr. Weber has relevant experience based on his previous tenure as acting Chief Executive Officer at Oculex (acquired by Allergan) and then Chief Executive Officer at MacuSight, both companies that were developing

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locally administered drug products for the eye. In October 2014, we announced the appointment of Anthony Yost as Chief Commercial Officer to prepare for the commercialization of AuriPro, if approved. Mr. Yost has 30 years of experience in pharmaceutical product sales and marketing, including senior management positions with Novartis AG, Innovex (a pharmaceutical sales and marketing services division of Quintiles Transnational Corporation), and Schering-Plough Corporation.

Our Strategy

Our objective is to develop and commercialize novel and best-in-class therapeutics to address unmet medical needs in the emerging otology market. The key elements of our strategy include:

Advance AuriPro Through Regulatory Approval and Pursue Development in Additional Indications. Our lead indication for AuriPro is the treatment of middle ear effusion in pediatric patients requiring TTP surgery. We believe this indication represents a significant area of unmet need, given that there are approximately one million TTP surgeries performed in the United States each year and no antibiotic ear drops are approved for this use. We have completed two identical Phase 3 clinical trials in a total of 532 pediatric patients. Results of these trials demonstrate that AuriPro achieved the primary efficacy endpoint with statistical significance ($p<0.001$) and that AuriPro was well tolerated. Based on these results, together with feedback received from a pre-NDA meeting and communications with the FDA and supportive results from the one year drug product stability testing required for filing, we submitted an NDA for AuriPro to the FDA in February 2015 seeking regulatory approval in the United States and, if approved within the standard review period, anticipate a commercial launch in the first quarter of 2016. We plan to assess and prioritize future potential therapeutic indications for AuriPro, including recurrent ear infections in patients with tympanostomy tubes, acute otitis externa, chronic suppurative otitis media (a perforated tympanic membrane with persistent drainage from the middle ear), and prophylaxis following middle ear surgeries, and initiate clinical trials in one or more of these indications during the first half of 2015.

Develop OTO-104 for Treatment of Ménière s Disease and Other Inner Ear Disorders. Ménière s disease is a debilitating disorder impacting more than 600,000 patients in the United States with no FDA-approved drug treatments. We are currently conducting a Phase 2b clinical trial for OTO-104 for patients with Ménière s disease that we expect will serve as one of two pivotal, single-dose trials required to demonstrate efficacy for an NDA submission in the United States. We announced in December 2014 that we had achieved the target patient enrollment in this trial and expect to report results in the second quarter of 2015. During October 2014, we began enrollment in a multiple-dose safety study in Ménière s patients in the United Kingdom. The prospective, randomized, placebo-controlled study, designed to evaluate the safety of multiple doses of OTO-104, will enroll 125 patients across multiple trial sites in the United Kingdom. We believe that the potential of OTO-104 for indications beyond Ménière s disease could also be substantial given the use of steroids for a broad range of otic disorders, such as sensorineural hearing loss, other balance disorders, and tinnitus.

Establish Our Own Sales and Marketing Capabilities to Commercialize Our Products in the United States. If approved, we plan to commercialize AuriPro, OTO-104 and other products in the United

States with our own focused, specialized sales force targeting approximately 5,000 ENTs who perform the majority of TTP surgeries and treat many of the patients with Ménière s disease, hearing loss, and tinnitus. Our initial target audience will comprise fewer than 2,500 ENTs who we believe perform approximately 80% of the TTP surgeries in the United States.

Maximize the Commercial Potential of Our Products Outside the United States. Since we have global commercialization rights to our product candidates, we are evaluating whether to develop and, if approved, commercialize our product candidates outside the United States on our own or in collaboration with partners. If we do enter into collaborations, our current preferred strategy is to

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establish broad collaborations with partners that have resources and interest for driving the development and commercialization of innovative therapeutics for the treatment of diseases and disorders of the ear.

Utilize Our Technology and Our Broad Patent Portfolio to Develop OTO-311 and Expand our Product Pipeline. We have a broad portfolio of issued patents and pending applications covering our product candidates as well as other potential applications of our technology in major markets around the world. We are developing OTO-311 for the treatment of tinnitus and will continue to evaluate new product opportunities to address significant unmet medical needs in otology. For example, one such area of great interest is the treatment of chronic hearing loss where considerable research in the field is underway to identify drugs that will preserve or improve hearing function.

Overview of Otology

The field of otology is a subspecialty within otolaryngology that focuses on diseases and disorders of the ear. The three main parts of the ear and common medical conditions for each are as follows:

Outer ear (*external region up to the tympanic membrane or ear drum*) infection or inflammation in this region is known as acute otitis externa, commonly referred to as swimmer s ear.

Middle ear (*cavity on the inner-side of the ear drum containing the three small bones or ossicles that transmit sound to the inner ear*) infection and inflammation in this area, known as otitis media, is a common occurrence in young children.

Inner ear (*compartment containing the cochlea for hearing and the vestibular organ for balance*) disorders associated with this region include balance disorders, such as Ménière s disease, as well as tinnitus and hearing loss.

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We estimate that more than 50 million people in the United States are affected by otic disorders and that approximately 20 million patients currently seek treatment each year for the most common conditions, including ear infections, balance disorders, tinnitus and hearing loss. As a result, we believe the existing market for treatments is significant and that there also remains a large population of untreated patients.

The American Academy of Otolaryngology Head and Neck Surgeons reports that approximately 2.5 million people in the United States are affected by acute otitis externa each year.

The National Institute on Deafness and Other Communications Disorders, or NIDCD, reports that three out of every four children experience otitis media by the time they are three years old.

According to the NIDCD, more than 600,000 patients have been diagnosed with Ménière s disease.

According to the American Tinnitus Association, approximately 16 million patients in the United States have tinnitus symptoms severe enough to seek medical attention, and about two million patients cannot function on a normal day-to-day basis. Furthermore, the United States Department of Defense reports that tinnitus accounts for the most prevalent service-connected disability among veterans and that the costs of service-related tinnitus are estimated to exceed $2 billion.

According to the NIDCD, approximately 36 million adults report some degree of hearing loss.

Current Otology Treatments and Limitations

Outer ear infections, such as acute otitis externa, or swimmer s ear, are typically treated with antibiotic ear drops and, in certain severe cases, oral antibiotics. If used properly, antibiotic ear drops are effective in resolving infections of the outer ear. However, treatment involves multi-dose, multi-day regimens, and incomplete compliance with such regimens may lead to clinical treatment failure and the recurrence of infection in some patients.

Middle ear infections, such as acute otitis media, are typically treated with oral antibiotics. However, this approach can result in systemic side effects and increased risk of bacterial resistance. Patients with persistent effusion or recurrent infections may be referred to an ENT for TTP surgery, during which tympanostomy tubes are inserted through the eardrum to ventilate the middle ear cavity. As the tympanostomy tube itself is frequently insufficient to treat the middle ear effusion, antibiotic ear drops are routinely used off-label during and following the procedure. Antibiotic ear drops are also used, and approved, for recurrent infections in patients with tympanostomy tubes. As with the outer ear, such antibiotic ear drop treatments involve multi-dose, multi-day regimens which can be problematic to follow, particularly in pediatric patients who represent the bulk of the TTP patient population.

Inner ear disorders, including balance disorders, tinnitus and hearing loss, represent an emerging field for drug treatment. Local drug delivery via direct injection through the ear drum has been demonstrated to offer a viable approach to address many disorders in this region since high drug levels can be achieved in the inner ear and systemic drug exposure is low. This injection, called an intratympanic, or IT, injection, allows for the delivery of drugs to the middle ear cavity through the ear drum, and then to the inner ear compartment via passage through the round window membrane. In clinical trials, favorable results have been reported with IT injection of steroids in patients with

Ménière s disease and sudden sensorineural hearing loss. However, a limitation of IT injection of solution-based formulations is their rapid elimination from the middle ear cavity down the Eustachian tube when the patient talks, swallows or sits up. The short time that the solution remains in contact with the round window membrane in the middle ear cavity limits the amount of drug that can pass into the inner ear and also limits the duration over which drug is retained in the inner ear. We believe that this reduces the therapeutic effect and increases treatment variability across patients. In an attempt to help mitigate this problem, ENTs require patients to remain immobilized for an extended period of time following each IT injection, and return for additional IT injections during the course of treatment. Despite these efforts, drug levels measured in the inner ear following IT injection of solution decrease rapidly and decline away from the round window membrane.

Given the compliance challenges of multi-dose, multi-day ear drop regimens for treating the middle ear, and anatomical barriers associated with achieving high and sustained drug levels in the inner ear via oral administration or an IT injection of solution, we believe that there is a large unmet medical need for improved otic drug delivery.

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Our Proprietary Otic Drug Delivery Technology

We have developed a proprietary formulation technology that provides sustained drug exposure in the middle or inner ear from a single local administration. Our technology utilizes a thermosensitive polymer, which transitions from a liquid to a gel at body temperature. The polymer is combined with drug microparticles to create a suspension that is retained in the middle ear cavity for an extended period of time. This prolonged residence time provides high and sustained drug exposure in the middle and inner ear. Potential benefits of our technology include:

- Provides full course of treatment from a single local administration thereby eliminating the need for repeat dosing as is required with solutions.
- Achieves high drug levels in the target location and minimizes systemic exposure.
- Provides high and sustained drug levels in the middle ear versus the pulsatile drug levels observed with antibiotic ear drops.
- Provides drug distribution throughout the inner ear compartment compared to solutions which result in declining drug levels away from the round window membrane.
- Eliminates the need for the patient to remain in a prone position for an extended period of time, improving patient acceptance and practice efficiency.
- Permits simple office-based administration by the ENT.
- Avoids potential issues with patient compliance and challenges in completing multi-dose, multi-day treatment regimens.

Our approach to address unmet needs in otology through optimized local drug delivery has been influenced by the rapid growth of intravitreal treatments for the eye. Like the ear, the eye is a protected sensory organ. Over the last two decades, ophthalmologists have demonstrated that injecting drugs into the eye can be done safely to treat debilitating visual disorders, such as age-related macular degeneration, or AMD. Drug therapies delivered via intravitreal injection revolutionized the treatment of AMD patients and created a multi-billion dollar market for the biopharmaceutical industry. Similar to ophthalmologists, ENTs are increasingly using locally administered drugs to treat both middle and inner ear conditions demonstrating the potential for multiple, significant new market opportunities for otology drug developers.

Our Product Candidates

The following table summarizes key information regarding our product candidate pipeline:

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AuriPro: Sustained-Exposure Antibiotic for Otic Indications

AuriPro is a sustained-exposure formulation of the antibiotic ciprofloxacin in development for the treatment of middle ear effusion in pediatric patients requiring TTP surgery. We have completed two randomized, prospective, double-blind, sham-controlled Phase 3 clinical trials with identical protocols that enrolled a total of 532 pediatric patients at approximately 60 centers in the United States and Canada. Results of these trials demonstrate that AuriPro achieved the primary efficacy endpoint, reduction in the incidence of treatment failures, with statistical significance ($p<0.001$) and that AuriPro was well tolerated. In these trials, AuriPro reduced the risk of treatment failure, as measured by the occurrence of post-operative otorrhea (drainage) or any use of rescue antibiotics, by an average of 49% in all randomized patients across the two trials, and the rate of post-operative otorrhea or use of rescue antibiotics for documented otorrhea or otitis media by an average of 62% in all randomized patients across the two trials (p£0.004), in each case as compared to sham. Based on these results, together with feedback received from a pre-NDA meeting and communications with the FDA and supportive results from the one year drug product stability testing required for filing, we submitted an NDA for AuriPro to the FDA in February 2015. If approved within the standard review period, we anticipate a commercial launch in the United States in the first quarter of 2016. We plan to assess and prioritize future potential therapeutic indications for AuriPro, including acute otitis media with tympanostomy tube in place, or AOMT, acute otitis externa, chronic suppurative otitis media, and prophylaxis following middle ear surgeries, and initiate clinical trials in one or more of these indications during the first half of 2015. We have global commercialization rights to AuriPro with patent protection in the United States until at least 2030.

Background on use of antibiotics for otic indications

Antibiotics are frequently used to treat otic infections with annual volume estimated to total approximately 21 million units per year in the United States. Of this total, approximately 13 million units are oral antibiotics. The remaining eight million units consist of antibiotic ear drops utilized in a number of clinical conditions. FDA-approved indications for antibiotic ear drops include acute otitis externa and AOMT. Antibiotic ear drops are also used off-label during and following TTP surgery and for various other middle ear conditions. In total, we estimate that approximately 2.3 million antibiotic ear drop units are used each year for the middle ear.

AuriPro for the treatment of otic indications

Of the various indications where antibiotic ear drops are currently used, we selected TTP surgery as the lead indication for AuriPro for the following reasons:

- There are approximately one million TTP surgeries performed each year in the United States and antibiotic ear drops are used in nearly all cases.

- Despite their routine use, no antibiotic ear drop has received FDA approval for this indication. If approved, we anticipate that AuriPro will be the first and only product labeled for this indication at the time of approval.

- A single-use, physician-administered product has significant advantages over multi-dose, multi-day ear drop regimens in this patient population because it avoids potential issues with compliance. More than half of TTP surgeries are performed in patients age three and under, and three-fourths are in children

age five and under. Administration of ear drops in young children can be very challenging for caregivers. This is compounded by the fact that current antibiotic ear drop products require multi-dose, multi-day regimens for efficacy. For example, CIPRODEX Otic s treatment regimen is twice daily dosing for seven days and ofloxacin, a generic antibiotic, is administered three-times daily for ten days. Full compliance with these multi-dose, multi-day regimens can be challenging, and missed antibiotic doses can compromise efficacy and increase the potential for bacterial resistance.

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We believe the physician audience for this indication can be addressed with a focused, specialized sales force. We estimate that fewer than 2,500 ENTs perform 80% of TTP surgeries in the United States. We therefore believe that promotion to this target group of physicians can be effectively achieved with a focused, specialized sales force.

We plan to assess and prioritize additional development opportunities for AuriPro, including AOMT, acute otitis externa, chronic suppurative otitis media, and prophylaxis following middle ear surgeries.

AuriPro product profile

AuriPro is a suspension containing the antibiotic ciprofloxacin and a thermosensitive polymer called Poloxamer 407 (P407), which exists as a liquid at or below room temperature and gels immediately upon transitioning to body temperature following administration. We selected ciprofloxacin since it is a broadly used antibiotic with activity against the bacterial pathogens common to otic infections and is present in several FDA-approved antibiotic ear drop products.

AuriPro has been formulated to provide sustained-exposure of ciprofloxacin so that a single administration provides a full course of treatment. There are two components that enable sustained-exposure of ciprofloxacin to the middle ear following administration, specifically the P407 and use of microparticles of ciprofloxacin. Immediately following injection, P407 gels thereby avoiding elimination down the Eustachian tube as is seen with solution-based formulations. Increasing residence time in the middle ear enables the localization and adherence of ciprofloxacin microparticles. The P407 gel remains in the middle ear for approximately one week and leaves behind ciprofloxacin microparticles that provide sustained-exposure for approximately one to two weeks.

Preclinical pharmacokinetic studies demonstrate that a single administration of AuriPro provides sustained-exposure of ciprofloxacin in the middle ear for approximately one to two weeks, as shown in the figure below. By comparison, repeat administration with CIPRODEX Otic ear drops through a tympanostomy tube results in drug levels that fluctuate considerably. Importantly, this preclinical pharmacokinetic study suggests that a single administration of AuriPro may provide higher cumulative drug exposure in the middle ear than the multi-dose, multi-day regimen of antibiotic ear drops.

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Based on this pharmacokinetic profile, efficacy in a standard preclinical model of otitis media, and supportive safety testing profile, we filed an IND and initiated a Phase 1b clinical trial in 2012.

AuriPro clinical development program for use during TTP surgery

We submitted an IND to the FDA in August 2011 to begin clinical development of AuriPro for the treatment of middle ear effusion in pediatric patients requiring tympanostomy tube placement. AuriPro has been the subject of one Phase 1b clinical trial and two Phase 3 clinical trials for this indication. Our clinical development strategy, originally presented to the FDA during pre-IND discussions in November 2010, contemplated progressing directly from a Phase 1b clinical trial to two Phase 3 pivotal studies pending our ability to demonstrate an acceptable safety profile in the target population in the Phase 1b clinical trial. Following our Phase 1b clinical trial, we met with the FDA in September 2013, designated as an End-of-Phase 2 meeting by the FDA, to review the results from the Phase 1b clinical trial and our development strategy to progress directly from Phase 1b to Phase 3, and to discuss the remaining requirements for submission of an NDA under Section 505(b)(2). Following the Phase 3 clinical trials, we completed pre-NDA communications with the FDA consisting of submitted questions and received responses related to clinical, non-clinical and file formatting matters and a face-to-face meeting related to Chemistry, Manufacturing, and Controls, or CMC, matters. Based on responses provided by the FDA, we do not anticipate that the FDA will require us to conduct additional studies to support a registration filing or that the FDA will convene an advisory committee meeting prior to approving AuriPro; however, we have no assurances from the FDA that additional studies or additional information will not be required to support a registration filing or approval. In December 2014, we commenced one year stability testing for AuriPro drug product and have received results that we believe are supportive of regulatory approval and commercialization. Based on the Phase 3 clinical trial results, feedback received from a pre-NDA meeting and communications with the FDA, and supportive results from the one year drug product stability testing required for filing, we submitted an NDA for AuriPro to the FDA in February 2015. Section 505(b)(2) 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. This regulatory approval pathway differs from submission of an NDA under Section 505(b)(1) where the data required for approval comes from studies conducted by or for the applicant or for which the applicant has obtained a right of reference.

AuriPro Phase 3 clinical trials

The Phase 3 clinical trial program consisted of two identical prospective, randomized, double-blind, sham-controlled, multicenter, studies of AuriPro given as a single IT injection for intra-operative treatment of middle ear effusion in pediatric patients requiring TTP surgery. As shown below, each trial consisted of two treatment arms, 6 mg AuriPro and no treatment (sham), with patients randomized 2 to 1, respectively.

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The primary endpoint of the Phase 3 clinical trials was the cumulative proportion of treatment failures defined as otorrhea (fluid draining through the tube) observed by a blinded assessor from Day 4 through the Day 15 visit, or use of rescue antibiotics from Day 1 through the Day 15 visit, whichever occurred first. Patients ages six months to 17 years were eligible for the clinical trial if they presented with effusion (fluid) in both ears (bilateral) at the time of TTP surgery. Following randomization, patients received either AuriPro or no treatment (sham). Treatment was administered in the operating room following the myringotomy (a small incision in the ear drum) and suctioning, and before the placement of the tube. As is customary in pediatric patients, all patients were under general anesthesia for the procedure. Follow-up visits occurred on Day 4, 8, 15 and 29 after surgery.

Enrollment in the AuriPro Phase 3 clinical trials commenced in November 2013 and was completed in April 2014. Approximately 60 trial sites in the United States and Canada participated, and a total of 532 pediatric patients were enrolled across the two clinical trials that were internally designated as Study 302 and Study 303. An analysis of the baseline patient demographics data from both trials suggests reasonable balance with no notable differences between the treatment groups. All enrolled patients completed the Day 15 study visit, except for one patient in a sham group and one patient in an AuriPro group who were randomized but not treated.

In early July 2014, we announced that the Phase 3 clinical trials had demonstrated that AuriPro achieved its primary efficacy endpoint as well as several secondary endpoints and was well tolerated. As the figure below indicates, AuriPro demonstrated a reduction for the primary efficacy endpoint, the incidence of treatment failures through Day 15 in all randomized patients, which averaged 49% across the two trials, in each case as compared to sham. This effect on the incidence of treatment failures was statistically significant ($p<0.001$) for both trials.

The p-value is the probability that the reported result was achieved purely by chance (e.g., a p-value £ 0.001 means that there is a 0.1% or less probability that the difference between the sham group and the treatment group is purely due to chance). A p-value £ 0.05 is a commonly used criterion for statistical significance and may be supportive of a finding of efficacy by regulatory authorities.

One sensitivity analysis performed on the primary endpoint, the per-protocol analysis, evaluated the incidence of treatment failures in all enrolled patients who did not have a major protocol deviation. More than 80% of patients in each trial and treatment group qualified for this analysis. As the figure below indicates, AuriPro provided a reduction in the rate of treatment failure through Day 15 in the per-protocol population averaging more than 60% across the two trials, in each case as compared to sham. This effect was statistically significant ($p<0.001$) for both trials.

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A post-hoc analysis was conducted that evaluated the cumulative proportion of patients in the Phase 3 trials considered treatment failures due to observation of otorrhea by the blinded observer or use of either otic or systemic antibiotics with documentation of otorrhea or otitis media through Day 15. The figure below presents this data for the Phase 3 trials which indicate that AuriPro reduced the rate of post-operative otorrhea or use of rescue antibiotics for documented otorrhea or otitis media by more than 60% when averaged across both trials, in each case as compared to sham. This effect was statistically significant in both trials (p£0.004).

AuriPro was well tolerated in the Phase 3 clinical trials. There were no deaths, no serious adverse events related to AuriPro, and no subjects were discontinued due to adverse events. There were no adverse findings demonstrated on physical examination or vital signs. Most adverse events were mild or moderate in severity. Safety assessments included treatment-emergent adverse events, or TEAEs, hearing function testing and tympanometry (middle ear function). Results for TEAEs are presented in the table below. Overall, there are no observed differences between AuriPro and sham treatment.

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Phase 3 Results: Treatment-Emergent Adverse Events

(Patients from Combined 302 and 303 Studies)

System Organ Class: Number of Patients (%)	Sham (N=174)	AuriPro (N=356)
Total patients with at least one TEAE reported	95 (54%)	189 (53%)
Infections and infestations	40 (23%)	85 (24%)
General disorders and administration site conditions	30 (17%)	62 (17%)
Gastrointestinal disorders	17 (10%)	41 (11%)
Respiratory, thoracic and mediastinal disorders	23 (13%)	38 (11%)
Injury, poisoning and procedural complications	20 (11%)	26 (7%)
Ear and labyrinth disorders	11 (6%)	25 (7%)
Skin and subcutaneous tissue disorders	4 (2%)	13 (4%)
All others	£2%	£2%

Note: two patients were randomized but not treated (one patient in the sham group and one in the AuriPro group)

Additionally, treatment with AuriPro was not found to have a negative impact on hearing, tympanometry or otoscopy (general examination of the ear), and there was no increase in the incidence of tube clogging with AuriPro.

Results from the Phase 3 clinical trials have been accepted for presentation at the American Society of Pediatric Otolaryngology spring meeting in April 2015.

AuriPro Phase 1b clinical trial

The single Phase 1b clinical trial, which evaluated AuriPro in pediatric patients with middle ear effusion requiring TTP surgery, had the same basic study design as the Phase 3 clinical trials discussed above. Two dose levels of AuriPro were evaluated relative to P407 gel vehicle (placebo) and no treatment (sham). A total of 83 patients were enrolled in the clinical trial (21 in the sham group, 22 in the placebo group, 21 in the 4 mg AuriPro group, and 19 in the 12 mg AuriPro group). An analysis of the baseline demographics data from these patients suggests reasonable balance with no notable differences between treatment groups. All enrolled patients, except one, completed the clinical trial. This one patient was considered lost to follow-up because he/she did not return to the trial site for the final visit.

A schematic outlining the design of the Phase 1b clinical trial is shown below. Patients ages 6 months to 12 years were eligible for the clinical trial if they presented with effusion in both ears at the time of TTP surgery. Following randomization, patients received one of two concentrations of AuriPro, the P407 gel vehicle (placebo) or no treatment (sham). Treatment was administered in the operating room following the myringotomy and suctioning, and before the placement of the tube. As is customary in pediatric patients, all patients were under general anesthesia for the procedure. All patients were treated and received tubes in both ears.

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Follow-up visits occurred on Day 4, 8, 15 and 29 after surgery. The primary endpoint for assessing clinical activity of AuriPro was the cumulative proportion of treatment failures defined as otorrhea observed by a blinded assessor from Day 4 through the Day 15 visit or use of rescue antibiotics from Day 1 through the Day 15 visit, whichever occurred first. Since the proportion of treatment failures was similar between the sham and placebo groups, these groups were combined into a single control group (sham/placebo) according to the pre-specified statistical analysis plan. As the figure below indicates, both the 4 mg and 12 mg AuriPro doses demonstrated a statistically significant reduction ($p<0.05$) in the incidence of treatment failures through Day 15 that exceeded 60%. The reduction in the proportion of treatment failures was similar between the two AuriPro dose levels as was expected based on the preclinical pharmacokinetic profile.

AuriPro was well tolerated in the Phase 1b clinical trial. There were no deaths in the clinical trial and no serious adverse events that were related to AuriPro treatment. There were no adverse findings demonstrated on physical examination or vital signs. Most adverse events were mild or moderate in severity. Safety assessments included TEAEs, including hearing function testing and tympanometry (middle ear function). Treatment with AuriPro was not found to have a negative impact on hearing, tympanometry, or otoscopy (general examination of the ear). Additionally, there was no evidence of tube clogging with AuriPro.

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AuriPro preclinical development program

In addition to the pharmacokinetic profiling studies summarized above, the AuriPro preclinical development program included pharmacological studies in established models of otitis media and otic safety testing.

The pharmacological profile of AuriPro was compared to antibiotic ear drops in a standard preclinical model of otitis media. This study demonstrated that a single administration of AuriPro reduced effusion volume and bacterial count to a level comparable to a multi-dose, multi-day regimen with antibiotic ear drops administered through a tympanostomy tube. In a subsequent study, AuriPro demonstrated a reduction in effusion volume and bacterial count even without the placement of a tube thereby highlighting the potential for AuriPro to address new clinical indications where multi-dose, multi-day antibiotic ear drops are not utilized today.

The preclinical safety program for AuriPro focused on ototoxicity and middle ear histology compared to multi-dose, multi-day antibiotic ear drops. In general, AuriPro s profile compared favorably to antibiotic ear drop products already approved by the FDA for other otic indications.

Potential market opportunity for AuriPro

The initial target market for AuriPro totals approximately one million TTP procedures conducted each year in the United States, for which multi-dose, multi-day antibiotic ear drops are routinely used off-label today. Based on a survey conducted in 2014, ENTs expressed strong interest in using AuriPro in these procedures once, and if, it becomes commercially available.

The survey, which we commissioned a third-party market research firm to conduct, consisted of an online interview of 100 ENTs who were screened to ensure that each participant performed a minimum of 25 TTP surgeries in the three months prior to the interview. Physicians who participated in our clinical trials of AuriPro were excluded from this survey. Overall, 55% of the ENTs screened were qualified to participate. During the interview process, each participant was presented a series of questions regarding their current practices with respect to TTP surgeries and various otic conditions, attitudes toward current treatments and areas of unmet need, and their reaction to a product profile and description of AuriPro. The participants relied solely on the AuriPro profile and description in responding to the questions presented in the study and no participant had prior experience with this product candidate. When asked to indicate the likelihood of using AuriPro during TTP procedures on a scale of 1 to 10, where 10 means extremely likely and 1 means not at all likely, 69% of the surveyed ENTs expressed a strong interest in using AuriPro by ranking their interest with an 8, 9 or 10. When participants were asked to rate AuriPro on various attributes such as safety, tolerability and frequency of complications, as compared to antibiotic ear drops, the AuriPro product profile was rated as better than antibiotic ear drops by more than 80% of respondents for compliance/adherence, approximately 50% of respondents for patient tolerability and achieving adequate drug exposure, and one-third or more of respondents for reducing the incidence of post-operative otorrhea, reducing the incidence of post-operative tube clogging and reducing the frequency of complications.

The survey is subject to various limitations, such as a small sample size, the hypothetical nature of the questions asked, the informal nature of the questions, the preliminary nature of the AuriPro profile used in the survey and other limitations, and therefore may not accurately reflect how ENTs will assess AuriPro or use it if it becomes commercially available in the future. Actual ENT adoption of AuriPro will also be affected by numerous factors outside the scope of the survey, including the safety and efficacy of AuriPro, the labeling of AuriPro, the extent to which ENTs become aware of AuriPro and its potential benefits, the perceived advantages and disadvantages of AuriPro relative to other products or treatments, the availability of adequate coverage and reimbursement for AuriPro and other factors including the risk factors related to AuriPro in the Risk Factors section of this Annual Report on

Form 10-K. As a result, we cannot predict to what extent ENTs will ultimately adopt AuriPro, if approved, in the future.

In addition to AuriPro s perceived product benefits, we also expect that our ability to actively promote and educate physicians regarding AuriPro will be an important competitive advantage over a multi-dose, multi-day regimen of antibiotic ear drops.

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We plan to assess and prioritize future potential therapeutic indications for AuriPro, including AOMT, acute otitis externa, chronic suppurative otitis media and prophylaxis following middle ear surgeries, and intend to initiate clinical trials in one or more of these indications during the first half of 2015.

OTO-104: Sustained-Exposure Steroid for Inner Ear Disorders

OTO-104 is a sustained-exposure formulation of the steroid dexamethasone in development for the treatment of Ménière s disease and other inner ear conditions. We are conducting a Phase 2b clinical trial at more than 50 centers in the United States and Canada to assess reductions in vertigo frequency and improvements in tinnitus in patients with Ménière s disease. We believe this trial will serve as one of two pivotal, single-dose efficacy trials required to support U.S. regulatory approval. In December 2014, we announced that we had achieved the target patient enrollment of 140 patients, and subsequently concluded enrollment with a total of 154 patients. We expect to report results from this clinical trial in the second quarter of 2015. If results are positive, we plan to initiate a second pivotal trial of OTO-104 in 2015. During October 2014, we began enrollment in a multiple-dose safety study in Ménière s patients in the United Kingdom. The prospective, randomized, placebo-controlled study, designed to evaluate the safety of multiple doses of OTO-104, will enroll 125 patients across multiple trial sites in the United Kingdom. In the first part of the study, patients will be randomized to receive two doses of either placebo or 12 mg OTO-104 by intratympanic (IT) injection given at three month intervals. Patients completing the double-blind portion of the study will be eligible to participate in an open-label extension study where all patients will receive two IT injections of OTO-104 at three month intervals. We intend to use data from this U.K. study together with one or more additional multiple-dose safety studies that we plan to initiate during 2015 to satisfy our multiple-dose clinical safety requirement for U.S. regulatory approval of OTO-104 in patients with Ménière s disease which we believe, based on discussions from an End-of-Phase 1 meeting with the FDA, will require 100 patients treated for one year and 300 patients treated for six months. The FDA has granted OTO-104 Fast Track designation, which is a process designed to facilitate the development and expedite the FDA s review of drugs to treat serious conditions and fill unmet medical needs. We have global commercialization rights to OTO-104 with patent protection in the United States until at least 2029.

Background on use of steroids for inner ear disorders

Multiple clinical and preclinical publications support the potential benefit of steroids to treat patients with a broad range of otic conditions including Ménière s disease, other balance disorders, sudden sensorineural hearing loss, other types of sensorineural hearing loss, and tinnitus. We estimate that there are over eight million patients treated each year in the United States for these inner ear disorders, and a similar if not larger population of patients in the European Union. Treatment with steroids includes both off-label oral dosing and IT injection regimens. Published clinical reports using IT steroids typically feature repeat injections per treatment regimen.

Background on 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. Of these symptoms, the vertigo attacks are typically most troubling for patients since they disrupt daily activities and are difficult to anticipate and manage. In general, patients are diagnosed with unilateral Ménière s disease in middle age and symptoms often continue for decades. Over time, the fluctuating hearing loss becomes permanent in many patients and a subset of patients will develop symptoms in their second ear. According to the NIDCD, there are more than 600,000 patients diagnosed with Ménière s disease in the United States.

The underlying cause of Ménière s disease is not well understood and there is no known cure. The pathophysiology is believed to involve fluid buildup in the inner ear compartment so the typical first line treatment in the United States is observance of a low-salt diet and off-label use of diuretics. Oral and IT steroids are used in a subset of Ménière s

patients who have persistent or severe symptoms. While treatment protocols vary greatly, the majority of published clinical trials with off-label use of steroid solution in Ménière s patients utilize repeat IT injections for each course of treatment. Patients who are unresponsive to steroid treatment may resort to surgical or chemical ablation, which can cause irreversible hearing loss.

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We selected Ménière s disease as the lead indication for OTO-104 in the United States for the following reasons:

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.

Ménière s patients often suffer a high level of disability and have very poor quality of life, especially during acute attacks.

Empirical evidence from physician-sponsored clinical trials suggests clinical benefit with the use of steroids.

FDA considers Ménière s disease to be a serious disorder. Accordingly, we applied for and were granted Fast Track designation for OTO-104.

As a chronic disorder, patients with Ménière s disease may suffer from episodic acute attacks and require repeat courses of treatment over their lifetime.

Symptom definitions developed by the American Academy of Otolaryngology Head and Neck Surgery provided the basis for the vertigo end point used in the evaluation of efficacy in our clinical program.

We plan to assess and prioritize additional opportunities for OTO-104 in conditions where ENTs currently use steroids off-label, including other balance disorders, sudden sensorineural hearing loss, other types of sensorineural hearing loss and tinnitus.

OTO-104 product profile

OTO-104 is a suspension containing the steroid dexamethasone in P407, which exists as a liquid at or below room temperature and gels immediately following an intratympanic, or IT, injection. OTO-104 has been formulated to provide sustained-exposure in the inner ear compartment such that a single IT injection provides a full course of treatment. This profile was demonstrated in our preclinical studies as summarized in the graphic below. These studies showed measurable dexamethasone levels in the inner ear fluid, or perilymph, more than one month after a single OTO-104 injection. By comparison, IT injection of steroid solution provides less than a day of drug exposure in the perilymph. From these studies, we advanced 2% and 6% OTO-104 concentrations into a Phase 1b clinical trial as the 3 mg and 12 mg dose, respectively.

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OTO-104 clinical development program for Ménière s disease

We submitted an IND to the FDA in December 2009 to begin clinical development of OTO-104 for the treatment of vertigo associated with Ménière s disease. Based on discussions from an End-of-Phase 1 meeting with the FDA, we believe that two pivotal, single-dose trials will be required to support efficacy of OTO-104 for Ménière s disease patients in an NDA submission. We are currently conducting a single-dose Phase 2b clinical trial that we expect to serve as one of the two pivotal trials. In December 2014, we announced that we had achieved the target patient enrollment of 140 patients and subsequently concluded enrollment with a total of 154 patients. Following successful completion of the Phase 2b clinical trial and an End-of-Phase 2 meeting with the FDA in 2015, we plan to initiate a second pivotal, single-dose Phase 3 clinical trial in approximately 140 patients.

In addition, based on discussions from an End-of-Phase 1 meeting we expect that the FDA will require multiple-dose clinical safety data in order to approve OTO-104 for use in Ménière s disease patients. During October 2014, we began enrollment in a multiple-dose safety study in Ménière s patients in the United Kingdom. The prospective, randomized, placebo-controlled study designed to evaluate the safety of multiple doses of OTO-104 will enroll 125 patients across multiple trial sites in the United Kingdom. In the first part of the study, patients will be randomized to receive two doses of either placebo or 12 mg OTO-104 by IT injection given at three month intervals. Patients completing the double-blind portion of the study will be eligible to participate in an open-label extension where all patients will receive two IT injections of OTO-104 at three month intervals. We intend to use data from this U.K. study together with one or more additional multiple-dose safety studies that we plan to initiate during 2015 to satisfy our multiple-dose clinical safety requirement for U.S. regulatory approval of OTO-104 in patients with Ménière s disease which we believe, based on discussions from an End-of-Phase 1 meeting with the FDA, will require 100 patients treated for one year and 300 patients treated for six months.

We have not yet conducted any multiple-dose clinical trials in the United States. Following completion of a Phase 1b clinical trial, the OTO-104 program was put on Full Clinical Hold due to adverse findings in a preclinical study evaluating the safety of repeated doses of OTO-104. We generated additional preclinical data, which was submitted to the FDA. OTO-104 was subsequently removed from Full Clinical Hold in July 2013, allowing for initiation of the current 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 preclinical data. We submitted additional preclinical data to the FDA and OTO-104 was removed from Partial Clinical Hold in June 2014.

OTO-104 Phase 2b clinical trial in Ménière s disease patients

We are currently conducting a Phase 2b clinical trial for patients with Ménière s disease at more than 50 centers in the United States and Canada. This trial is a prospective, randomized, double-blind, placebo-controlled Phase 2b clinical trial designed to assess the efficacy and safety of OTO-104 for the treatment of Ménière s disease in a total of 140 patients. In December 2014, we announced that we had achieved the target patient enrollment of 140 patients, and subsequently concluded enrollment with a total of 154 patients. The clinical trial has been designed and is being conducted to serve as one of the two pivotal, single-dose efficacy trials we expect that the FDA will require to support an NDA filing for treatment of Ménière s disease patients.

The primary endpoint of the Phase 2b clinical trial is the reduction in vertigo frequency during Month 3 following treatment compared to a one month baseline period. This endpoint is identical to the one used in the Phase 1b clinical trial and reviewed with the FDA at an End-of-Phase 1 meeting. The trial size was determined in order to provide 90% power to achieve statistical significance ($p<0.05$) for a 30% treatment effect which was the level observed in the Phase 1b clinical trial. Tinnitus is being assessed as an exploratory endpoint in the clinical trial. The clinical trial will also assess the safety and tolerability of a single IT injection of OTO-104.

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Upon screening, all patients enter into a one month observational period for a baseline assessment during which they record their vertigo and tinnitus symptoms via a daily diary. Following the lead-in period, eligible patients are randomized 1:1 to a single IT injection of 12 mg OTO-104 or P407 gel vehicle (placebo). Patients are observed for up to four months following treatment with Month 3 (weeks 9 through 12) used to evaluate efficacy versus placebo.

A schematic of the clinical trial design is shown in the figure below:

We expect to announce results in the second quarter of 2015.

OTO-104 Phase 1b clinical trial in Ménière s disease patients

We have completed a randomized, prospective, double-blind, placebo-controlled, multicenter, Phase 1b clinical trial of a single IT injection of OTO-104 in patients with Ménière s disease. A total of 44 patients were enrolled and completed the clinical trial. The Phase 1b clinical trial design was generally the same as the ongoing Phase 2b clinical trial, except that two different doses of OTO-104, 3 mg or 12 mg, were evaluated relative to P407 gel vehicle (placebo), and patients were observed for three months following treatment. The primary endpoint for efficacy was vertigo frequency during Month 3 compared to baseline. This is the same primary endpoint used in the ongoing Phase 2b clinical trial.

OTO-104 was well tolerated in the Phase 1b clinical trial when administered as a single IT injection of 3 mg or 12 mg. There were no serious adverse events observed during the clinical trial. There were no instances of persistent conductive hearing loss associated with OTO-104 injection. Protocol pre-specified Adverse Events of Interest, or AEIs, reported during the clinical trial included injection site perforation of the tympanic membrane, a single 12 mg patient reporting vertigo during the procedure, and a single placebo patient with serous otitis media. Of these AEIs, only injection site perforation of the tympanic membrane was reported in more than a single patient. These perforations were predominantly described as pinhole perforations observed following IT injection of OTO-104. Most of these perforations resolved spontaneously, and all but one of these resolved by the end of the clinical trial. In general, the safety events were consistent with those reported in published clinical trials with the use of IT injections of steroids.

Although the Phase 1b clinical trial was not designed to establish efficacy due to the relatively small number of patients enrolled in the trial, trends with respect to the clinical activity of OTO-104 were observed. As the graphic below indicates, the 12 mg OTO-104 group experienced a mean reduction of vertigo frequency from baseline totaling 73% in Month 3 compared to 56% for 3 mg OTO-104 and 42% for placebo. This provides a treatment benefit of 12 mg OTO-104 versus placebo of approximately 30%. In absolute terms, the 12 mg OTO-104 group achieved a reduction in days with vertigo episodes from eight during baseline to two in Month 3.

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We have also assessed the Phase 1b clinical trial results using a patient responder analysis. As shown in the graphic below, 81% of patients in the 12 mg OTO-104 group realized at least a 50% improvement in vertigo frequency in Month 3 versus baseline, compared to 71% for 3 mg OTO-104 and 50% of patients receiving placebo.

In addition to the observed effect on vertigo, OTO-104 was associated with improvement in tinnitus, as measured by the Tinnitus Handicap Inventory (THI-25). THI-25 is a patient questionnaire that provides a measure of the impact of tinnitus on a patient s functional status. The average score at baseline was 52-58 for the three treatment groups corresponding to a Moderate Handicap grade. As shown in the figure below, the mean change of THI-25 total score from baseline to Month 3 totaled 15 for the 12 mg OTO-104 group, 12 for 3 mg OTO-104 and 4 for patients receiving placebo. Furthermore, the level of change experienced by patients in the 12 mg OTO-104 group moved the average handicap level of the group from Moderate grade at baseline to Mild in Month 3. THI-25 is being assessed as an exploratory endpoint in the Phase 2b clinical trial.

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In summary, the Phase 1b clinical trial in Ménière s disease patients demonstrated that OTO-104 is well tolerated when administered as a single IT injection, and there were no serious adverse events observed during the clinical trial. Based on the observation of persistent pinhole perforations in this trial, we modified the topical anesthetic used to numb the ear drum in the ongoing Phase 2b clinical trial. Although the Phase 1b clinical trial size was small, the results demonstrate that 12 mg of OTO-104 was associated with a clinically meaningful improvement in both vertigo frequency and tinnitus endpoints compared to placebo three months after treatment. Based on these results, we selected 12 mg OTO-104 for advancement into late-stage testing for Ménière s disease.

OTO-104 preclinical development program

In addition to the pharmacokinetic profiling studies summarized above, the OTO-104 preclinical development program included pharmacological studies in established hearing loss models and extensive safety testing.

Since there are no preclinical models of Ménière s disease, we conducted studies to evaluate pharmacological activity of a single IT injection of OTO-104 in standard models of acute onset hearing loss. In particular, we have demonstrated that OTO-104 provides a protective effect when given before exposure to loud noise or ototoxic chemotherapeutic agents. Furthermore, administration of OTO-104 within two to three days following exposure to acoustic trauma promotes hearing recovery. These findings are consistent with published data for steroids, and supported dose selection for the Phase 1b clinical trial.

The preclinical safety program for OTO-104 has focused on ototoxicity since the side effect profile of systemic dexamethasone in humans is well characterized, and the level of systemic exposure from an IT injection is minimal. Ototoxicity testing has included single- and multiple-dosing studies of OTO-104 in a number of species. We submitted preclinical data to the FDA and OTO-104 was subsequently removed from Partial Clinical Hold in June 2014.

Potential market opportunity for OTO-104

The initial target market for OTO-104 is the more than 600,000 patients diagnosed with Ménière s disease in the United States. Based on a survey conducted in 2014, ENTs expressed strong interest in using OTO-104 to treat patients with Ménière s disease.

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The survey, which we commissioned a third-party market research firm to conduct, consisted of an online interview of 100 ENTs who were screened to ensure that each participant treated a minimum of four patients with Ménière s disease in the month prior to the interview. Physicians who participated in our clinical trials of OTO-104 were excluded from this survey. Overall, 66% of the ENTs screened were qualified to participate. During the interview process, each participant was presented a series of questions regarding their current practices for treatment of patients with Ménière s disease, attitudes toward current treatments and areas of unmet need, and their reaction to a product profile and description of OTO-104. The participants relied solely on the OTO-104 profile and description in responding to the questions presented in the study and no participant had prior experience with this product. When asked to indicate the likelihood of using OTO-104 to treat patients with Ménière s disease on a scale of 1 to 10, where 10 means extremely likely and 1 means not at all likely, 57% of the surveyed ENTs expressed a high likelihood in using OTO-104 by ranking their interest with an 8, 9 or 10.

The survey is subject to various limitations, such as a small sample size, the hypothetical nature of the questions asked, the informal nature of the questions, the preliminary nature of the OTO-104 profile used in the survey, and other limitations, and therefore may not accurately reflect how ENTs will assess OTO-104 or use it if it becomes commercially available in the future. Actual ENT adoption of OTO-104 will also be affected by numerous factors outside the scope of the survey, including the safety and efficacy of OTO-104, the labeling of OTO-104, the extent to which ENTs become aware of OTO-104 and its potential benefits, the perceived advantages and disadvantages of OTO-104 relative to other products or treatments, the availability of coverage and adequate reimbursement for OTO-104 and other factors including the risk factors related to OTO-104 in the Risk Factors section of this Annual Report on Form 10-K. As a result, we cannot predict to what extent ENTs will ultimately adopt OTO-104, if approved, in the future.

We expect that with approval of OTO-104 and patient education the market opportunity will expand over time. We plan to assess and prioritize additional opportunities for OTO-104 in conditions where ENTs currently use steroids off-label, including other balance disorders, sudden sensorineural hearing loss, other types of sensorineural hearing loss, and tinnitus.

OTO-311: Sustained-Exposure Treatment for Tinnitus

OTO-311 is a sustained-exposure formulation of the NMDA receptor antagonist gacyclidine in development for the treatment of tinnitus. Historic and emerging clinical data generated by third parties support the use of NMDA receptor antagonists, including gacyclidine, as potential treatments for tinnitus. We plan to file an IND with the FDA for OTO-311 and initiate a Phase 1 clinical trial in 2015. In November 2014, we announced the completion of an exclusive license agreement with Ipsen that enables us to use clinical and non-clinical gacyclidine data generated by Ipsen to support worldwide development and regulatory filings for OTO-311. We have global commercialization rights to OTO-311 with patent protection in the United States until at least 2031.

Background on tinnitus

Tinnitus is the medical term for hearing noise when there is no outside source of the sound. It is often described as a ringing in the ear but can also sound like roaring, clicking, hissing or buzzing. The American Tinnitus Association reports that approximately 16 million patients in the United States have tinnitus symptoms severe enough to seek medical attention, and about two million patients cannot function on a normal day-to-day basis. Furthermore, the United States Department of Defense reports that tinnitus accounts for the most prevalent service-connected disability among veterans and that the costs of service-related tinnitus are estimated to exceed $2 billion.

While the most common cause of tinnitus is exposure to loud noise, a number of other factors can be involved including heart or blood vessel problems, hormonal changes in women, ear and sinus infections, certain medications and thyroid problems. 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 treating this debilitating condition.

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Background on NMDA receptor antagonists for tinnitus

Historic and emerging clinical data provide support for the use of NMDA receptor antagonists 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. For example, Auris Medical Holding AG reported improvement in several patient reported outcome measures, including tinnitus loudness and tinnitus severity, in a subset of patients treated in a Phase 2 clinical trial with repeat IT injections of AM-101, a formulation of the NMDA receptor antagonist esketamine, and Merz Pharmaceuticals GmbH reported an improvement in the tinnitus handicap index in a Phase 2 clinical trial with the oral NMDA receptor antagonist neramexane. We expect that the results of these and additional ongoing trials will be instructive in the design and implementation of the clinical development program for our single-administration OTO-311 product candidate.

Background on gacyclidine

Gacyclidine is a potent and selective NMDA receptor antagonist. Receptor binding studies have demonstrated potency and selectivity against the NMDA receptor subtype believed to be relevant for tinnitus, and biological activity has been demonstrated in a preclinical model of tinnitus. In addition, studies in preclinical models of neuroprotection have demonstrated a broad therapeutic window for activity versus neurotoxicity. Finally, binding studies indicate that gacyclidine s dissociation kinetics are slower than some other NMDA receptor antagonists which could be beneficial in achieving sustained drug levels in the inner ear following a single IT injection.

Although never approved or commercialized, gacyclidine has been evaluated in clinical trials that we believe will be helpful to our development of OTO-311. The molecule was originally developed by Ipsen for the treatment of traumatic brain and spinal cord injury in the late 1990 s. These clinical trials evaluated systemic dosing of gacyclidine in over 300 patients from which they established a maximum tolerated dose, or MTD. Although we expect limited systemic exposure with IT injection of OTO-311, we believe the reported MTD provides a useful upper limit for our dose selection activities. In November 2014, we announced the completion of an exclusive license agreement with Ipsen that enables us to use clinical and non-clinical gacyclidine data generated by Ipsen to support worldwide development and regulatory filings for OTO-311.

Recent third-party pilot clinical trials with local administration of gacyclidine delivered using a micro-pump and indwelling catheter have been conducted in patients with tinnitus. While not sized to demonstrate efficacy, we believe based on published results from one study conducted by Wenzel et al. in Germany and data from a second study that we have acquired from NeuroSystec that the trials provide evidence of clinical activity for gacyclidine in modulating aspects of the tinnitus symptoms experienced by patients.

Based partly on these prior clinical efforts, we acquired assets and patent rights related to gacyclidine which we intend to leverage in our development of OTO-311 for tinnitus. From an affiliate of the NeuroSystec Corporation, we acquired data and intellectual property generated during their development program. In a related transaction, we completed a license agreement with DURECT Corporation, or Durect, that gives us exclusive rights to a patent family directed to the use of gacyclidine for the treatment of tinnitus. This patent family has issued patents in the United States and Japan. We also have our own issued patents and pending applications directed to a sustained-exposure gacyclidine product that we expect will lengthen and broaden the coverage for OTO-311 provided by the licensed patent.

OTO-311 development program

The goal of the OTO-311 program is to develop a sustained-exposure formulation of gacyclidine that will provide a full course of treatment from a single IT injection. Following pre-IND meeting communications with the FDA, we plan to file an IND with the FDA for OTO-311 and initiate a Phase 1 clinical trial in 2015. We anticipate the design and execution of our clinical development program will benefit from the results of tinnitus clinical trials in the field.

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Potential market opportunity for OTO-311 in tinnitus

We believe the treatment of tinnitus represents a significant market opportunity since the patient population is large, symptom severity can be debilitating, and there are currently no FDA-approved drug treatments. If our development program is successful and OTO-311 is approved by the FDA, then we plan to market this product to ENTs with the same focused, specialized sales force that will be promoting our other approved product candidates.

Competition

We expect to enter the highly competitive biopharmaceutical market. 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.

AuriPro

Antibiotic ear drops are currently the primary treatment option for middle ear effusion during TTP surgery. The leading branded antibiotic ear drop is CIPRODEX Otic from Alcon, a division of the Novartis Group. However, no antibiotic ear drop has been approved by the FDA for this use and the effectiveness of this current treatment option relies on patient compliance for the full course of the multi-dose, multi-day regimen. The key competitive factors affecting the success of AuriPro, if approved, 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. We are also aware that Alcon recently received FDA approval for a new antibiotic ear drop for use in treating acute otitis externa and may evaluate this product for various other otic indications, and that Otic Pharma Ltd. has a foam-based formulation of ciprofloxacin that is in clinical development for otic indications potentially including use during TTP surgery.

OTO-104

There are no drugs currently approved by the FDA for the treatment of Ménière s disease. Current treatments commonly used for Ménière s disease 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 Synphora AB is conducting a Phase 2/3 clinical trial with a formulation of latanoprost administered via single or repeat IT injections, and that Auris Medical Holding AG has indicated it intends to evaluate AM-111 in an open-label study of Ménière s patients.

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OTO-311

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 Phase 3 clinical trials evaluating repeat IT injections of AM-101 in patients with acute and post-acute inner ear tinnitus, Autifony Therapeutics, which has initiated Phase 2 testing for their oral product candidate for tinnitus, Merz Pharmaceuticals GmbH, which has suspended development of oral neramexane for chronic tinnitus while its partner in Japan, Kyorin Pharmaceuticals Co., continues with a Phase 2 clinical trial for tinnitus, and Novartis AG, which has completed a Phase 2 clinical trial for chronic tinnitus.

Sales and Marketing

In October 2014, we announced the appointment of Anthony Yost as Chief Commercial Officer to prepare for the commercialization of AuriPro, if approved, including the hiring of a sales and marketing team. Mr. Yost has 30 years of experience in pharmaceutical product sales and marketing, including senior management positions with Novartis AG, Innovex (a pharmaceutical sales and marketing services division of Quintiles Transnational Corporation) and Schering-Plough Corporation. Assuming receipt of regulatory approval for AuriPro, and successful completion of clinical trials and receipt of regulatory approval for our other product candidates, we plan to commercialize AuriPro, OTO-104, OTO-311 and any other approved products in the United States with our own focused, specialized sales force targeting approximately 5,000 ENTs who perform the majority of TTP surgeries and treat many of the patients with Ménière s disease, hearing loss, and tinnitus. We believe that promotion to this target group of physicians can be effectively achieved with a focused sales force.

For AuriPro, we expect that our initial target audience will comprise fewer than 2,500 ENTs who we believe perform approximately 80% of the TTP surgeries in United States. For OTO-104, we expect our initial target audience will be approximately 4,000 ENTs who account for approximately 80% of the prescription volume for the pharmaceutical class most frequently prescribed by ENTs, of whom a subset will also be targets for AuriPro.

Outside of the United States, we plan to evaluate whether to commercialize our products on our own or in collaboration with partners.

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.

AuriPro

We expect AuriPro to be reimbursed as a physician-administered drug in the United States. Our preliminary estimate for pricing of AuriPro is in the range of $200 to $250 per unit which is sufficient for treating both ears of a single patient. We expect this pricing to represent a premium to CIPRODEX Otic, the leading branded ear drop product, which has a current reported Wholesale Average Cost of approximately $159 per unit which is sufficient for a full course of treatment. We will conduct formal pricing research including testing with facilities and payors, prior to finalizing pricing for AuriPro. In order for physicians to use AuriPro, we will need to have the product available in

hospital outpatient facilities and ambulatory surgery centers, or ASCs, where the majority of pediatric TTP procedures are performed.

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The stocking of AuriPro in hospital outpatient facilities and ASCs will most likely require approval from hospital pharmacy and therapeutic committees and ASC administrators, respectively. The review by hospital pharmacy and therapeutic committees typically considers the product profile, clinical safety and efficacy results, current treatments used for the indication, level of interest/advocacy by the physician user base, and impact on facility economics. This process can require up to a year to complete and approval is uncertain. The time and requirements for approval by ASC administrators will likely vary by center and depend on a number of factors including level of interest / advocacy by the physician user base and impact to the facility economics. As an FDA-approved, physician-administered medication, we expect that AuriPro will be assigned a unique J-Code. This could facilitate reimbursement on a cost plus basis for those facilities that contract with insurers on a fee for service basis. However, obtaining a unique J-Code for AuriPro may not provide incremental reimbursement for facilities that are reimbursed a fixed amount for performing the TTP surgery. As part of the AuriPro commercial launch plan, we expect to implement a comprehensive set of programs that support the value proposition of AuriPro with facility administrators and payors.

OTO-104

Reimbursement for OTO-104 is expected to be separate from the IT injection procedure itself and based on the product s average selling price, which we currently project will be in excess of $1,000 per treatment. Because we expect OTO-104 will be determined to be therapeutically distinct from any other J-Code drug, we expect that the product will be assigned a unique J code. This will simplify billing and enable electronic adjudication by payors according to the average selling price. If OTO-104 is approved by the FDA, we plan to devote considerable resources to the training and education of office-based billing personnel regarding the appropriate coding for OTO-104 use.

Manufacturing

We currently contract with third parties for the manufacture, testing and storage of our 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. We expect third-party manufacturers to be capable of providing sufficient quantities of our 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 current product candidates is P407, a thermosensitive polymer. We currently purchase P407 from a single supplier on a purchase-order basis and we do not have a long-term 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, if approved for marketing by the applicable regulatory authorities, our commercial requirements.

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AuriPro

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

OTO-104

OTO-104 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 OTO-104 is approved for marketing by the applicable regulatory authorities, our commercial requirements. We currently use two third-party contract manufacturers to produce OTO-104 that we believe can satisfy our clinical requirements. We are currently evaluating our supply chain for the commercial manufacture of OTO-104.

OTO-311

OTO-311 is a suspension containing gacyclidine and P407. As OTO-311 is in preclinical development, we have not yet selected a manufacturer for the raw material or finished goods supply.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our 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 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 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 Risk Factors Risks Related to Our Intellectual Property.

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Our patent estate includes patents and applications with claims directed to our AuriPro, OTO-104 and OTO-311 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 through our proprietary technology. Our patent estate, on a worldwide basis, includes approximately 60 issued patents and allowed patent applications, and at least 85 pending patent applications with claims relating to our AuriPro, OTO-104, OTO-311, future product candidates, manufacturing processes and alternative otic delivery technologies.

For AuriPro, we co-own a patent family with The Regents of the University of California, or UC, that is directed to the composition and therapeutic use of AuriPro. Through an exclusive license agreement, we have acquired UC s rights in this patent family. This family includes one issued U.S. patent and three pending U.S. applications. The expiry date of the U.S. patent, without extensions, is April 2030, and this patent and any future U.S. patents issuing from the related applications are expected to be Orange Book (OB) listable. This family also includes issued patents or allowed applications in Australia, Canada, Israel, Korea, Philippines, Russia, South Africa and Taiwan; and pending applications in Argentina, Brazil, China, Europe, India, Japan, Jordan, Mexico, Pakistan, Singapore, 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 AuriPro. Finally, we have filed a solely owned U.S. provisional application directed to manufacturing methods of AuriPro.

For OTO-104, we co-own a patent family with UC directed to the composition and therapeutic use of OTO-104. Through an exclusive license agreement, we have acquired UC s rights in this patent family. This family includes five issued U.S. patents and one pending U.S. application. The expiry dates of the U.S. patents, without extensions, range from May 2029 to September 2029, and these patents and any future U.S. patent issuing from this application are expected to be OB listable. This family also includes issued patents or allowed applications in Australia, Canada, China, Hong Kong, Japan, Korea, Mexico, Peru, Russia, Singapore, South Africa, Taiwan and UK; and pending applications in Argentina, Brazil, Chile, Europe, India, Indonesia, Israel, Jordan, Malaysia, Pakistan, Philippines, Thailand, Uruguay, Venezuela and Vietnam. 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 OTO-104. Finally, we solely own an issued U.S. patent directed to manufacturing methods of OTO-104. The expiry date of this U.S. patent, without extensions, is April 2030.

For OTO-311, we co-own two patent families with UC directed to the composition and therapeutic use of OTO-311. Through an exclusive license agreement, we have acquired UC s rights in both patent families. These families include one issued U.S. patent and one allowed U.S. application. The expiry date of the U.S. patent, without extensions, is April 2031, and this patent and any future U.S. patent issuing from this application are expected to be OB listable. These families also include issued patents or allowed applications in Australia, Canada, China, Korea, Mexico, Russia, South Africa, Taiwan and UK; and pending applications in Argentina, Brazil, Chile, Europe, India, Israel, Japan, Jordan, Pakistan, Thailand, Uruguay and Venezuela. Divisional patent applications have been filed in select countries for those families. In addition, we have licensed from Durect a patent family directed to the therapeutic use of OTO-311. 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 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 a patent family 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-311, 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.

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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, or the 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 filed for trademark registration at the USPTO for AuriPro and ProAuric . 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 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. For more information, please see 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 which 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 our current and future product candidates. Under the agreement, UC reserved the right to use the patents and applications for its and other nonprofit institutions research and educational purposes.

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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 milestone payments of up to $2.7 million per licensed product, of which $0.9 million has been paid for AuriPro and $0.3 million has been paid for OTO-104 (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 AuriPro, OTO-104, and OTO-311. For more information, please see 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-311 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, or 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

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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-311. For more information, please see 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, or 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 preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA s current good laboratory practice, or cGLP, regulations;

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submission to the FDA of an IND which must become effective before clinical trials may begin;

approval by an independent institutional review board, or 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, or 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.

Preclinical Studies

Preclinical 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 preclinical 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 preclinical 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, or 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

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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 preclinical 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, or 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, or 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.

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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 OTO-104 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 preclinical 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. We intend to utilize the Section 505(b)(2) NDA pathway for our AuriPro product candidate.

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

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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

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injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label, 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, or 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, or 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, or 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 preclinical 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

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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 European Union 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. European Union 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, or ACA, contains provisions that have the

potential to substantially change healthcare delivery and financing, including impacting the profitability of drugs. For example, the Affordable Care Act revised the methodology by which rebates owed by manufacturers to the state and federal government for covered outpatient

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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, or 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 Affordable Care Act requires manufacturers of drugs, devices, biologicals and medical supplies to annually report to the Centers for Medicare & Medicaid

Services, or CMS, an agency within the U.S. Department of Health and Human Services, or 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.

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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.

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 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 European Union, 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

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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 $31.8 million and $16.3 million in research and development expenses in the years ended December 31, 2014 and 2013, respectively. From our inception through December 31, 2014, we have incurred an aggregate of approximately $75.7 million of research and development expenses, the significant majority of which relate to our development of AuriPro and OTO-104.

Employees

As of December 31, 2014, we had 38 full-time employees, including 29 employees engaged in research and development. 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.

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 entitled 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 clinical-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

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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 not obtained any regulatory approvals for any of our product candidates, commercialized our product candidates or generated any revenue. We continue to incur significant research and development and other expenses related to our ongoing clinical trials and operations. We have recorded net losses of $42.9 million, $19.6 million and $7.6 million for the years ended December 31, 2014, 2013 and 2012, respectively. As of December 31, 2014, we had an accumulated deficit of $102.5 million.

We currently have no source of product revenue and may never become profitable.

We expect to continue to incur significant losses for the foreseeable future. Our ability to achieve 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 therefore may never generate revenue that is significant or large enough to achieve profitability. 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 (deficit) 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 will require substantial additional financing to commercialize AuriPro and to obtain regulatory approval for OTO-104 and OTO-311, 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 our product candidates, AuriPro, OTO-104 and OTO-311. In particular, obtaining regulatory approval for and commercializing AuriPro, and commencing and completing clinical trials for OTO-104 and OTO-311, 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, 2014, we had cash, cash equivalents and short-term investments of $156.0 million. We believe that we will continue to expend substantial resources for the foreseeable future for the commercialization of AuriPro and the development of OTO-104, OTO-311 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 preclinical 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 timing of regulatory approval for AuriPro;
- the cost of commercialization activities if our products are approved for sale, including marketing, sales and distribution costs and related facilities expansion costs;

the timing of, and the costs involved in, clinical development and obtaining regulatory approvals for OTO-104, OTO-311 or any future product candidates;

the cost of manufacturing our products;

the number and characteristics of any other product candidates we develop or acquire;

our ability to establish and maintain strategic collaborations, licensing or other commercialization arrangements and the terms and timing of such arrangements;

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the degree and rate of market acceptance of any 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, including litigation costs and the outcome of such litigation;

the timing, receipt and amount of sales of, or royalties on, future approved products, if any; and

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 establishment of sales and marketing, manufacturing or distribution capabilities or other activities that may be necessary to commercialize our product candidates, preclinical 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 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 develop and commercialize our product candidates or operate as a business.

Risks Related to Our Product Candidates

We are substantially dependent on the regulatory and commercial success of our lead product candidate, AuriPro.

To date, we have invested substantial resources in the development of our lead product candidate, AuriPro. AuriPro is our only product that has completed Phase 3 clinical development.

Given the completion of our Phase 3 clinical trials for AuriPro, its future success is primarily subject to the risks associated with obtaining regulatory approval from the FDA and commercialization, including risks associated with:

the eligibility of AuriPro for the Section 505(b)(2) regulatory approval pathway which could potentially simplify the FDA approval process;

the FDA s acceptance of our NDA submission for AuriPro;

the FDA requiring additional studies or information to support our submission;

the successful and timely receipt of necessary marketing approval from the FDA to allow us to begin commercializing AuriPro in the United States;

the ability to manufacture commercial supplies of AuriPro;

our ability to build a sales organization to market AuriPro;

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our success in educating physicians, patients and caregivers about the benefits, administration and use of AuriPro;

the availability, perceived advantages, relative cost, relative safety and relative efficacy of other products or treatments for middle ear effusion at the time of TTP surgery, particularly the off-label use of multi-dose, multi-day antibiotic ear drops;

the demand for the treatment of middle ear effusion in patients requiring TTP surgery;

the availability of coverage and adequate reimbursement for AuriPro;

our ability to enforce our intellectual property rights in and to AuriPro; and

a continued acceptable safety profile of AuriPro 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 successfully obtain regulatory approval of, commercialize or generate significant revenue from AuriPro. If we cannot do so, or are significantly delayed in doing so, our business will be materially harmed.

We are also dependent upon the clinical, regulatory and commercial success of OTO-104, our second product candidate.

In addition to AuriPro, we have also invested substantial resources in the development of our second product candidate, OTO-104. OTO-104 is currently in a Phase 2b clinical trial and is our only other product candidate in clinical trials. We expect to report results for this clinical trial in the second quarter of 2015 and, if the results are positive, initiate a Phase 3 clinical trial thereafter. We have initiated a multiple-dose safety study for OTO-104 in Ménière s patients in the United Kingdom and plan to initiate one or more additional multiple-dose safety studies during 2015 to satisfy our multiple-dose clinical safety requirement for U.S. regulatory approval of OTO-104 in Ménière s patients.

Given the stage of development of OTO-104, it is currently most subject to the risks associated with completing its current clinical trials and future clinical trials, including risks associated with:

the completion of enrollment of the ongoing Phase 2b clinical trial for OTO-104;

the use of patient reported outcomes in our Phase 2b clinical trial;

our ability to demonstrate the safety and efficacy of OTO-104 in this clinical trial;

the FDA s willingness to accept the results of our Phase 2b clinical trial as one of two pivotal, single-dose efficacy trials required to support regulatory approval;

the successful implementation, enrollment and completion of a second pivotal, single-dose efficacy trial that demonstrates the safety and efficacy of OTO-104;

the successful implementation, enrollment and completion of one or more additional open-label safety studies and the ongoing multiple-dose safety study in the United Kingdom; and

the ability to file an NDA for regulatory approval with the FDA without the need for any additional clinical trials.

If we are able to successfully complete the necessary clinical trials for OTO-104, its success will still remain subject to the risks associated with obtaining regulatory approval from the FDA and being commercialized, including risks associated with:

the timing of review, as the FDA s grant of Fast Track designation for OTO-104 does not guarantee priority review;

the FDA s acceptance of our NDA submission for OTO-104;

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the successful and timely receipt of necessary marketing approval from the FDA to allow us to begin commercializing OTO-104 in the United States;

the ability to manufacture commercial supplies of OTO-104;

the ability of our future sales organization to sell OTO-104;

our success in educating physicians and patients about the benefits, administration and use of OTO-104;

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 OTO-104;

our ability to enforce our intellectual property rights in and to OTO-104; and

a continued acceptable safety profile of OTO-104 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 OTO-104 further through final clinical development, or obtain regulatory approval of, commercialize or generate significant revenue from OTO-104. If we cannot do so, or are significantly delayed in doing so, our business will be materially harmed.

In addition to AuriPro and OTO-104, our long-term prospects depend in part upon advancing additional product candidates, such as OTO-311, into clinical development and through to regulatory approval and commercialization.

Although we are focused upon potential regulatory approval and commercialization of AuriPro and completion of the clinical trials and potential regulatory approval and commercialization of OTO-104, the development of OTO-311 and other potential candidates for the treatment of inner and middle ear disorders is a key element of our long-term strategy. OTO-311 is currently in preclinical development and is therefore currently most subject to the risks associated with preclinical 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 a clinical trial;

enrolling sufficient numbers of 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-311 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-311 or any other future product candidate.

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Risks Related to Our Business and Strategy

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

We have in the past experienced delays in our ongoing 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 preclinical, 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 trial;
- identify, recruit and train suitable clinical investigators;
- reach agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites;
- obtain and maintain institutional review board, or IRB, approval at each clinical trial site;
- identify, recruit and enroll suitable patients to participate in a trial;
- have a sufficient number of patients complete a trial or return for post-treatment follow-up;
- ensure clinical investigators observe trial protocol or continue to participate in a trial;

address any patient safety concerns that arise during the course of a 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

raise sufficient capital to fund a trial.

Patient enrollment is a significant factor in the timing of clinical trials and 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 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 trial or by the FDA or any other regulatory authority, or if the IRBs of the institutions

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in which such 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.

OTO-104 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 current Phase 2b clinical trial. As a result of OTO-104 being placed on Full Clinical Hold, AuriPro was also placed on Full Clinical Hold. The AuriPro 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.

If we experience delays in the completion of, or termination of, any clinical trial of our product candidates for any reason, 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. 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 adequately demonstrates the safety and efficacy of the product for the intended indication. We have not yet obtained regulatory approval to market any of our 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 preclinical 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 preclinical or clinical trials are required;

the FDA s non-approval of the formulation, labeling or the specifications of our product candidates;

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the FDA s failure to accept the manufacturing processes or facilities of third-party manufacturers with which we contract; 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.

Even if AuriPro, OTO-104, OTO-311 or any future product candidates obtain regulatory approval, they may fail to achieve the broad degree of market acceptance and use necessary for commercial success.

Even if we obtain FDA or other regulatory approvals, our products may not achieve market acceptance among physicians and patients, and may not be commercially successful. There are currently no FDA-approved drug treatments for the indications we are pursuing. Middle ear effusion in pediatric patients requiring TTP surgery, our proposed indication for our lead candidate AuriPro, is currently treated with the off-label use of antibiotic ear drops. Our proposed indication for OTO-104 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-311 is the treatment of tinnitus. Currently, physicians may attempt to treat tinnitus symptoms with the off-label use of steroids, anxiolytics, antidepressants, and antipsychotics. The commercial success of 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 AuriPro for middle ear effusion in pediatric patients requiring TTP surgery, or to elect to utilize OTO-104 for Ménière s disease or OTO-311 for tinnitus, 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 a new treatment in lieu of other products or treatments;

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, including persistent injection site perforation of the tympanic membrane, which has occurred in our OTO-104 Phase 1b clinical trial;

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;

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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

general patient or caregiver confidence, which may be impacted by economic and political conditions.

If our product candidates are approved for use but 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.

Use of our product candidates could be associated with side effects or adverse events.

As with most pharmaceutical products, use of our 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 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 or market our product candidates. Side effects such as toxicity or other safety issues associated with the use of our product candidates could require us to perform additional studies or halt development or sale of these product candidates or expose us to product liability lawsuits which will harm our business. We may be required by regulatory agencies to conduct additional preclinical or clinical trials regarding the safety and efficacy of our 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 AuriPro and OTO-104. For example, one patient in our Phase 1b clinical trial of OTO-104 experienced a persistent injection site perforation of the tympanic membrane. If we are successful in commercializing our product candidates, the FDA and other foreign regulatory agency regulations will require that we 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 products. 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.

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 AuriPro, the current use of antibiotic ear drops to treat middle ear effusion in patients requiring TTP surgery. We are also aware that other companies, such as

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Auris Medical Holding AG, Autifony Therapeutics, Kyorin Pharmaceuticals, Merz Pharmaceuticals GmbH, Novartis AG, Otic Pharma Ltd. and Synphora AB, are conducting clinical trials for potential products for the treatment of various otic indications, including ear infections, tinnitus and Ménière s disease. 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 candidates.

We rely on third parties to conduct many of our preclinical 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 preclinical 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 which we rely are required to comply with Good Clinical Practice, or 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 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 material produced under current Good Manufacturing Practice, or 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 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 preclinical and clinical drug supplies and we intend to rely on third parties to produce commercial supplies of any approved products.

We outsource the manufacture of our product candidates. We do not currently have the infrastructure or internal capability to manufacture supplies of our product candidates for use in development and commercialization. If we were to experience an unexpected loss of supply of our product candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, 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 a product candidate, or the raw material components thereof, for an ongoing clinical trial due to the need to replace a contract manufacturer or other third-party manufacturer could considerably 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 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 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 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 candidates or if it withdraws any such acceptance in the future, we may 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 candidates that we may develop 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

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.

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As we commercialize our products, we may encounter issues with manufacturing.

Our product candidates have never been manufactured for commercial use, and 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 raw materials. Even if we could otherwise obtain regulatory approval for our product candidates, there is no assurance that our contract manufacturers will be able to manufacture the approved product to specifications acceptable to the FDA or foreign regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product or to meet potential future demand. If our contract manufacturers are unable to produce sufficient quantities of the 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 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 all of our product candidates, ciprofloxacin for AuriPro, dexamethasone for OTO-104, and gacyclidine for OTO-311, 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 candidates, we may need to engage alternate suppliers to prevent a possible disruption of the manufacture of the materials necessary to produce our product candidates for our clinical trials, and if approved, ultimately for commercial sale. 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, the commercialization of AuriPro and the development of OTO-104, OTO-311 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 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.

We are currently developing AuriPro for the treatment of middle ear effusion in pediatric patients requiring TTP surgery and OTO-104 for the treatment of vertigo associated with Ménière s disease. Although at an earlier stage, we plan to develop OTO-311 for the treatment of tinnitus. The FDA and other applicable regulatory agencies will restrict our ability to market or 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, and if approved, promote and commercialize new treatment indications for our products in the future, but we cannot predict when or if we will receive the regulatory approvals required to do so. Failure to receive such approvals prevents us from promoting or 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, 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, if we receive marketing approval for AuriPro for treatment of middle ear effusion in pediatric patients requiring TTP surgery, the first indication we are pursuing, we cannot promote the use of our product in a manner that is inconsistent with the approved label. However, physicians are able to, in their independent medical judgment, use AuriPro 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 FDA has 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 FDA 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. If our products are misused or used with improper technique, we may become subject to 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 covering our clinical trials 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 currently have limited marketing capabilities and no sales organization. If we are unable to establish sales and marketing capabilities on our own or through third parties, we will be unable to successfully commercialize our products, if approved, or generate product revenue.

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

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

As of December 31, 2014, we had 38 full-time employees, including 29 employees engaged in research and development. As we advance our product candidates through the development process and to commercialization, we will need to continue to expand our development, regulatory, quality, managerial, sales and marketing, operational, finance and other resources to manage our operations and clinical trials, continue our development activities and commercialize our product candidates, if approved. As our operations expand, we expect that we will need to manage additional relationships with various manufacturers and collaborative partners, suppliers and other organizations.

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

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. We cannot be certain that coverage and adequate reimbursement will be available for any of our products, if approved, or that such coverage and reimbursement will be authorized in a timely fashion. Also, we cannot be certain that reimbursement policies will not reduce the demand for, or the price paid for, any of our products, 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, if any, 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.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation established Medicare Part D, which expanded Medicare coverage for outpatient prescription drug purchases by the elderly but provided authority for limiting the number of drugs that will be covered in any therapeutic class. The MMA also introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. Any negotiated prices for any of our products, if approved, covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain outside of the Medicare Part D prescription drug plan. Moreover, while Medicare Part D applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment under Medicare Part D may result in a similar reduction in payments from non-governmental payors.

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 is 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 the initiatives that 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 Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act (collectively, ACA), became law in the United States. The goal of

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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 predict what impact on federal reimbursement policies this legislation will have in general or on our business specifically, the ACA may result in downward pressure on pharmaceutical reimbursement, which could negatively affect market acceptance of any of our products, if they are approved. 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;

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 beginning in 2014, 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.

The ACA may change in the future.

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 will face an even greater risk if we commercialize any products. 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

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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 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 covering our clinical trials 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 due to the commercial launch of any approved product, 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 and when we obtain approval for marketing our product candidates, we intend to expand our insurance coverage to include the sale of the applicable products;

however, we may be unable to obtain this liability insurance on commercially reasonable terms.

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, 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.

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.

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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 three product candidates, a key element of our strategy is to identify, develop and commercialize additional product candidates for the treatment of inner and middle ear diseases and 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.

Despite the implementation of security measures, our internal computer systems and those of our CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced a material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs.

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, 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 area and we have a small office space in Alamo, California, each of which in the past has experienced severe earthquakes. We do not carry earthquake

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insurance. The San Diego area has also recently 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 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, such as the most recent global financial crisis which caused extreme volatility and disruptions in the capital and credit markets, 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. 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 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 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.

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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 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 candidates. Furthermore, even if they are unchallenged, our patents may not adequately protect our product candidates, provide exclusivity for our 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 candidates is challenged, it could dissuade companies from collaborating with us to develop, or threaten our ability to commercialize our 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 candidates, we may be open to competition from generic versions of our 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 candidates under patent protection would be reduced.

Almost all 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, or the 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 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 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 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

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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 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, or 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. The USPTO is currently developing regulations and procedures to govern administration of the AIA, and many of the substantive changes to patent law associated with the AIA. 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 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 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 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 developing 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

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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 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 fields 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 candidates may give rise to claims of infringement of the patent rights of third parties. We cannot assure you that our product candidates will not infringe existing or future patents owned by third parties. We may not be aware of patents that have already issued that a third party, for example a competitor in the otic market, might assert are infringed by our 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 candidates, could be found to be infringed by our 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 and commercialize our product candidates. 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 and commercialize our product candidates, 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.

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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 candidates, the defendant could counterclaim that the patent covering our 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 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 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 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.

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If we fail to comply with our obligation 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 candidates is exclusively in-licensed from DURECT Corporation, or Durect, which license includes a sublicense to patents jointly owned by Durect and the Institut National de la Sante et de la Recherche Medicale, or 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-311, which would adversely affect our ability to proceed with any development or potential commercialization of OTO-311, and could subject us to claims of patent infringement by Durect if OTO-311 is covered by the licensed patents.

In addition, a significant portion of our patent portfolio for our product candidates was co-developed and is co-owned with The Regents of the University of California, or 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, patent prosecution and maintenance 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. 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 AuriPro, OTO-104 and OTO-311. While we could still proceed with development and, if approved, commercialization of AuriPro, OTO-104 and OTO-311 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.

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 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, or DEA, the Centers for Disease Control and Prevention, or CDC, the U.S. Department of Health and Human Services, and its various agencies, and also from foreign regulatory authorities. Failure to comply with all applicable regulatory requirements, including those promulgated under the Federal Food, Drug, and Cosmetic Act, or FFDCA, and, 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, 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, or 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 AuriPro, OTO-104, OTO-311 or any future 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. We have not obtained marketing approval for our product candidates anywhere in the world. 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;

civil and criminal penalties;

injunctions;

withdrawal of approved products;

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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 preclinical 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 preclinical studies and clinical trials can be interpreted in different ways, and insufficient or adverse results from preclinical studies can affect the ability to conduct clinical trials. For example, following completion of a Phase 1b clinical trial, the OTO-104 program was put on Full Clinical Hold due to adverse findings in a preclinical study evaluating the safety of repeated doses of OTO-104. OTO-104 was subsequently removed from Full Clinical Hold in July 2013, allowing for initiation of the current 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 preclinical data. We submitted additional preclinical data to the FDA and OTO-104 was removed from Partial Clinical Hold in June 2014. As a result of OTO-104 being placed on Full Clinical Hold, AuriPro was also placed on Full Clinical Hold. The AuriPro 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 preclinical 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 preclinical studies and clinical trials. The number of preclinical 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 preclinical studies and clinical trials sufficient;

the FDA might not accept our third-party manufacturers processes or facilities; or

the FDA may change its approval policies or adopt new regulations.

If AuriPro does not gain regulatory approval or OTO-104, OTO-311 or any future 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.

If the FDA does not conclude that AuriPro satisfies the requirements for the Section 505(b)(2) regulatory approval pathway, or if the requirements for approval of AuriPro under Section 505(b)(2) are not as we expect, the development and approval of AuriPro will likely take significantly longer, cost significantly more and entail significantly greater complexity and risks than anticipated, and in any case may not be successful.

We are seeking FDA approval through the Section 505(b)(2) regulatory pathway for AuriPro. Section 505(b)(2) of the FFDCA permits the submission of an NDA where some or all of the data required for

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approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. Our ability to rely on certain of the FDA s findings of safety and effectiveness in approval of another NDA or on studies published in the scientific literature will depend on our ability to demonstrate the relevance to AuriPro. We may be required to conduct additional studies or provide additional information to fully demonstrate the safety and effectiveness of our modifications to the approved product.

By pursuing the Section 505(b)(2) regulatory pathway for AuriPro, our reliance on the prior FDA findings of safety and effectiveness of the reference product may require any approved labeling for AuriPro to include certain information that is included in the labeling of the reference product.

If the FDA disagrees with our position that reliance on data for the reference product is appropriate, or if the data required for approval of our Section 505(b)(2) NDA are different than anticipated, we may need to conduct additional development activities, provide additional data and information, and meet additional standards for regulatory approval. If this were to occur, the time and financial resources required to obtain FDA approval for AuriPro would likely substantially increase. Moreover, the inability to pursue the Section 505(b)(2) regulatory pathway could result in new competitive products reaching the market faster than AuriPro, which could materially adversely impact our competitive position and prospects.

In addition, our competitors may file citizens petitions with the FDA in an attempt to persuade the FDA that our product candidates, or the clinical trials that support their approval, contain deficiencies. Such actions by our competitors could delay or even prevent the FDA from approving any NDA that we submit under Section 505(b)(2).

Even if we receive regulatory approval for 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, 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, 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 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 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;

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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, independent contractors, clinical investigators, CROs, consultants and vendors in connection with our current and future business activities are 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 the 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.

The federal False Claims Act, or 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.

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

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Our operations will also be subject to the federal transparency requirements under the Affordable Care Act, which requires manufacturers of drugs, devices, biologicals and medical supplies to annually report to the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, or 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.

If any of our business activities, including but not limited to our relationships with healthcare providers, 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. Also, 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 products. 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.

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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.

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.

Prior to our initial public offering, there was no public market for our common stock. An active trading market for our shares may never develop or, if developed, may not be sustained. 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 may 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;
- 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;
- variations in 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 future competitors;

changes in financial estimates or guidance, including our ability to meet our future revenue and operating profit or loss 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;

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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 analysts 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, 2014, we had 21,173,270 shares of common stock outstanding, approximately 11,536,595 of which are subject to 90-day lock-up agreements entered into in connection with our follow-on public offering that expire on April 22, 2015. Following the expiration of the lock-ups (or earlier if permitted by the managing underwriters), all shares of our common stock, will be eligible for sale in the public market, subject in some cases to the volume and other restrictions of Rule 144 under the Securities Act of 1933, as amended, or the Securities Act, as well as our insider trading policy. In addition, shares issued or issuable upon exercise of options and warrants vested as of the expiration of the lock-up period may be eligible for sale at that time. Sales of our common stock by current stockholders may make it more difficult for us to sell equity or equity-related securities in the future at a time and price that we deem reasonable or appropriate, and make it more difficult for you to sell shares of our common stock.

In addition, on August 13, 2014, we filed a registration statement on Form S-8 registering 2,093,580 shares of common stock reserved for issuance pursuant to awards outstanding under our Amended and Restated 2010 Equity Incentive Plan, 2,606,875 shares of common stock reserved for issuance pursuant to future awards under our 2014 Plan, and 380,000 shares reserved for issuance pursuant to future awards under our ESPP. Shares registered under this registration statement on Form S-8 will be available for sale in the public market subject to vesting arrangements and the exercise of such options, the lock-up arrangements described above and, in the case of our affiliates, the restrictions of Rule 144. As of December 31, 2014, options to purchase 959,232 shares of our common stock were exercisable.

Certain holders of approximately 13,415,846 shares of our common stock, including shares issuable upon the exercise of outstanding options and warrants, are entitled to certain rights with respect to the registration of their shares under the Securities Act, subject to the 90-day lock-up arrangement described above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares 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.

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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.

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. If we issue 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.

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

As of January 31, 2015, our executive officers, directors and current beneficial owners of 5% or more of our common stock, in aggregate, beneficially owned approximately 56.9% of our outstanding common stock.

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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

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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 to 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, 2014 we had U.S. federal and California net operating loss carryforwards, or NOLs, of approximately $60.5 million and $59.4 million, respectively, which expire in various years beginning in 2030, if not utilized. As of December 31, 2014, we had federal and California research and development tax credit carryforwards of approximately $2.8 million and $1.6 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, or the 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 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.

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, or NASDAQ, may increase legal and financial compliance costs and make some

activities more time consuming. These laws, regulations and standards are

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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, or 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. We expect that our first report on compliance with Section 404 will be furnished in connection with our financial statements for the year ending 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, 2014 or for any other period. Accordingly, no such opinion was expressed.

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 stock exchanges, 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 expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. These factors could also 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.

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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, 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 $1.0 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 is located in San Diego, California, where we occupy an approximately 14,500 square foot facility. The current term of our lease on this facility expires in February 2017. We have an option to extend this lease by an additional five years, which would extend our lease through February 2022. We expect that we will expand our facilities in order to accommodate our anticipated growth in connection with our commercialization efforts and that additional space will be available on commercially reasonable terms.

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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.

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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:

Quarter	High	Low
Third quarter ended September 30, 2014 (beginning August 13, 2014)	$ 28.20	$ 15.19
Fourth quarter ended December 31, 2014	$ 40.45	$ 19.86

Holders of Record

On March 9, 2015, the closing sale price of our common stock on The NASDAQ Global Select Market was $36.77. As of March 9, 2015, there were approximately 59 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.

Information About 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

In 2014, we sold unregistered securities as described below. Share amounts have been retroactively adjusted for the 35.16-for-1 reverse stock split effected on July 31, 2014.

On April 23, 2014, we sold an aggregate of 4,126,080 shares of series D convertible preferred stock at a per share purchase price of $11.96 pursuant to a series D preferred stock purchase agreement for aggregate cash proceeds to the Company of approximately $49.3 million.

In August 2014, we issued an aggregate of 228,902 shares of common stock that were not registered under the Securities Act to investors pursuant to the cash and net exercise of warrants at an exercise price of $8.79 per share, for aggregate cash proceeds to the Company of approximately $1.2 million.

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From January 1, 2014 through August 13, 2014 (the date of the filing of our registration statement on Form S-8, File No. 333-198116), pursuant to the terms of our Amended and Restated 2010 Equity Incentive Plan, we issued an aggregate of 57,870 shares of common stock that were not registered under the Securities Act to employees, a former employee and a director pursuant to the exercise of stock options at a weighted-average exercise price of $2.52 for cash proceeds of approximately $145,696.

In 2014, we granted stock options under our equity incentive plans to purchase an aggregate of 1,543,830 shares of our common stock at exercise prices ranging between $1.76 and $34.12 per share to a total of 41 employees, directors, officers and consultants.

None of the foregoing transactions involved any underwriters, underwriting discounts or commissions, or any public offering, and each transaction was deemed to be exempt from the registration requirements of the Securities Act, in reliance on (i) Section 4(2) of the Securities Act (or Regulation D promulgated thereunder) as transactions by an issuer not involving any public offering or (ii) Rule 701 promulgated under Section 3(b) of the Securities Act as transactions pursuant to compensatory benefit plans and contracts relating to compensation as provided under Rule 701. The recipients of the securities in each of these transactions represented their intentions to acquire the securities for investment only and not with a view to or for sale in connection with any distribution thereof and appropriate restrictive legends were placed upon the stock certificates issued in these transactions.

Use of Proceeds

On August 12, 2014, our Registration Statement on Form S-1 (File No. 333-197365) was declared effective by the SEC for our initial public offering of common stock. We started trading on The NASDAQ Global Select Market on August 13, 2014, and the transaction formally closed on August 18, 2014. In connection with the IPO, we issued 7,187,500 shares of common stock, including exercise of the underwriters option to purchase an additional 937,500 shares, at an offering price of $16.00 per share. J.P. Morgan Securities LLC, Merrill Lynch, Pierce, Fenner & Smith Incorporated, Piper Jaffray & Co. and Sanford C. Bernstein & Co. LLC acted as the underwriters. We received aggregate proceeds of approximately $104.1 million, net of underwriting discounts, commissions and offering-related transaction costs incurred. There has been no material change in the planned use of proceeds from our initial public offering as described in our final prospectus filed with the SEC on August 13, 2014 pursuant to Rule 424(b).

On January 22, 2015, our Registration Statement on Form S-1 (File No. 333- 201401) was declared effective by the SEC for our follow-on public offering of common stock. The transaction formally closed on January 28, 2015. In conjunction with the offering, we issued 2,932,500 shares of common stock, including exercise of the underwriters option to purchase an additional 382,500 shares, at an offering price of $29.25 per share. J.P. Morgan Securities LLC, Piper Jaffray & Co., Cowen and Company, LLC and Sanford C. Bernstein & Co. LLC acted as the underwriters. We received aggregate proceeds of approximately $80.0 million, net of underwriting discounts, commissions and offering-related transaction costs. There has been no material change in the planned use of proceeds from our public offering as described in our final prospectus filed with the SEC on January 23, 2015 pursuant to Rule 424(b).

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

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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, 2014. 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,		
	2014	2013	2012
Statements of Operations Data:			
Operating expenses:			
Research and development	$ 31,803	$ 16,336	$ 8,523
General and administrative	7,836	3,514	2,408
Total operating expenses	39,639	19,850	10,931
Loss from operations	(39,639)	(19,850)	(10,931)
Other (expense) income	(3,238)	291	3,362
Net loss and comprehensive loss	(42,877)	(19,559)	(7,569)
Accretion to redemption value of convertible preferred stock	(35)	(539)	(801)
Net loss attributable to common stockholders	$ (42,912)	$ (20,098)	$ (8,370)
Net loss per share attributable to common stockholders, basic and diluted	$ (5.46)	$ (268.79)	$ (118.99)
Weighted-average shares used to compute net loss per share attributable to common stockholders, basic and diluted	7,853,228	74,772	70,343

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	As of December 31, 2014	2013
Balance Sheets Data:		
Cash and cash equivalents	$ 139,810	$ 37,284
Short-term investments	16,223	
Working capital	152,285	36,298
Total assets	159,164	39,757
Convertible preferred stock warrant liability		646
Convertible preferred stock		95,153
Accumulated deficit	(102,469)	(59,557)
Total stockholders equity (deficit)	153,613	(58,977)

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 clinical-stage biopharmaceutical company focused on the development and commercialization of innovative therapeutics for the treatment of diseases and disorders of the ear. To overcome many of the limitations of delivering drugs to the middle and inner ear, we have developed a proprietary technology that is 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. Utilizing this technology, we have advanced three product candidates into development: AuriPro, OTO-104 and OTO-311.

AuriPro is a sustained-exposure formulation of the antibiotic ciprofloxacin for which we have completed two identical Phase 3 clinical trials in 532 pediatric patients with middle ear effusion requiring tympanostomy tube placement, or TTP, surgery. Results of these Phase 3 trials demonstrate that AuriPro achieved the primary efficacy endpoint with statistical significance ($p<0.001$) and that AuriPro was well tolerated. Based on these results, together with feedback received from a pre-NDA meeting and communications with the U.S. Food and Drug Administration, or FDA, and supportive results from the one year stability testing required for filing, we submitted a New Drug Application, or NDA, for AuriPro to the FDA in February 2015. If approved within the standard review period, we anticipate a commercial launch for AuriPro in the United States in the first quarter of 2016.

OTO-104 is a sustained-exposure formulation of the steroid dexamethasone in development for the treatment of Ménière s disease and other inner ear conditions. We are conducting a Phase 2b clinical trial at more than 50 centers in the United States and Canada, which we believe will serve as one of two pivotal, single-dose efficacy trials required to support U.S. regulatory approval. In December 2014, we announced that we had achieved the target patient enrollment of 140 patients, and subsequently concluded enrollment with a total of 154 patients. We expect to report results from this clinical trial in the second quarter of 2015. If results are positive, we plan to initiate a second pivotal trial of OTO-104 in 2015. During October 2014, we began enrollment in a multiple-dose safety study in Ménière s patients in the United Kingdom. The prospective, randomized, placebo-controlled study, designed to evaluate the safety of multiple doses of OTO-104, will enroll 125 patients across multiple trial sites in the United Kingdom. In the first part

of the study, patients will be randomized to receive

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two doses of either placebo or 12 mg OTO-104 by intratympanic, or IT, injection given at three month intervals. Patients completing the double-blind portion of the study will be eligible to participate in an open-label extension study where all patients will receive two IT injections of OTO-104 at three month intervals. We intend to use data from this U.K. study together with one or more additional multiple-dose safety studies that we plan to initiate during 2015 to satisfy our multiple-dose clinical safety requirement for U.S. regulatory approval of OTO-104 in patients with Ménière s disease which we believe, based on discussions from an End-of-Phase 1 meeting with the FDA, will require 100 patients treated for one year and 300 patients treated for six months. The FDA has granted OTO-104 Fast Track designation, which is a process designed to facilitate the development and expedite the FDA s review of drugs to treat serious conditions and fill unmet medical needs.

OTO-311 is a sustained-exposure formulation of the N-methyl-D-aspartate receptor antagonist gacyclidine in development for the treatment of tinnitus. We plan to file an Investigational New Drug application, or IND, for OTO-311 with the FDA and initiate a Phase 1 clinical trial during 2015. In November 2014, we announced the completion of an exclusive license agreement with Ipsen that enables us to use clinical and non-clinical gacyclidine data generated by Ipsen to support worldwide development and regulatory filings for OTO-311.

We have global commercialization rights to our product candidates. Our strategy is to advance our product candidates through regulatory approval and self-commercialize in the United States. In October 2014, we announced the appointment of an experienced Chief Commercial Officer to prepare for the commercialization of AuriPro, if approved. We plan to build a focused sales force targeting ENTs, who specialize in the treatment of patients affected by diseases and disorders of the ear. Outside the United States, we plan to evaluate whether to commercialize our products on our own or in collaboration with partners. We have a broad patent portfolio of more than 60 issued patents and allowed patent applications and at least 85 pending patent applications covering our product candidates and indications, as well as other potential applications of our technology in major markets around the world.

We have a limited operating history. Since our inception in 2008, we have devoted substantially all of our efforts to developing our product candidates, including conducting preclinical and clinical trials and providing general and administrative support for these operations. We do not have any approved products and have not generated any revenue from product sales or otherwise.

From inception to December 31, 2014, we have raised net cash proceeds of approximately $143.8 million from the sale of convertible preferred stock, convertible notes and warrants. In August 2014, we completed our initial public offering, or IPO, in which we sold 7,187,500 shares of common stock at an offering price of $16.00 per share, which included the exercise in full by the underwriters of their option to purchase up to 937,500 additional shares of common stock. Proceeds from the IPO were approximately $104.1 million, net of underwriting discounts, commissions and offering-related transaction costs incurred. As of December 31, 2014, we had cash, cash equivalents and short-term investments of $156.0 million.

In January 2015, we completed a follow-on public offering of 2,932,500 shares of our common stock, which includes the exercise in full by the underwriters of their option to purchase 382,500 shares of common stock, at an offering price of $29.25 per share. Proceeds from the follow-on public offering were approximately $80.0 million, net of underwriting discounts, commissions and offering-related transaction costs.

We have never been profitable, and as of December 31, 2014, we had an accumulated deficit of $102.5 million. Our net losses were $42.9 million, $19.6 million and $7.6 million for the years ending December 31, 2014, 2013 and 2012, respectively. Substantially all of our net losses have resulted from costs incurred in connection with our development programs and from general and administrative costs associated with our operations.

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

- file for regulatory approval and prepare for commercialization of AuriPro in the United States;
- conduct our clinical development program for OTO-104;
- complete preclinical development and initiate clinical development of OTO-311;
- contract to manufacture our product candidates;
- evaluate opportunities for development of additional product candidates;
- maintain and expand our intellectual property portfolio;
- hire additional staff, including clinical, scientific, operational, financial, sales and marketing and management personnel, to execute our business plan; and
- operate as a public company.

We will need substantial additional funding to support our operating activities, especially as we approach the potential commercial launch of AuriPro in the United States and as we build our sales and marketing capabilities. We anticipate that our existing cash and cash equivalents and short-term investments, together with the net proceeds from our follow-on public offering completed in January 2015, will not be sufficient for us to commercialize AuriPro, register and commercialize OTO-104, and complete clinical development of OTO-311. Accordingly, we will continue to require substantial additional capital. The amount and timing of our future funding requirements 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 begin commercializing AuriPro. We anticipate that we will seek to fund our operations 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, together with the net proceeds from our follow-on offering completed in January 2015, will be sufficient to fund our currently planned operations for 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 annual license maintenance payments until we commercialize the first product covered

under the license agreement, development milestone payments of up to $2.7 million per licensed product, of which $0.9 million has been paid for AuriPro and $0.3 million has been paid for OTO-104 (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-311 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

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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

To date, we have not generated any revenue. We do not expect to generate any revenue from any product candidates that we develop unless and until we obtain regulatory approval and commercialize our products or enter into collaborative agreements with third parties. In the future, if AuriPro is approved for commercial sale in the United States, we may generate revenue from product sales. We do not expect to commercialize AuriPro before 2016, if ever.

Operating Expenses

Research and development expenses

Our research and development expenses primarily consist of costs associated with the preclinical and clinical development of our product candidates. 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 CROs in connection with our 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 products 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) by product candidate:

	Years Ended December 31,		
	2014	2013	2012
Third-party development costs:			
AuriPro	$ 10,510	$ 5,712	$ 2,394
OTO-104	10,793	3,510	1,290
OTO-311	1,986	46	
Total third-party development costs	23,289	9,268	3,684
Other unallocated internal research and development costs	8,514	7,068	4,839
Total research and development costs	$ 31,803	$ 16,336	$ 8,523

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We expect our research and development expenses to increase substantially for the foreseeable future as we pursue expanded indications for AuriPro and advance our other product candidates through their respective clinical development programs. The process of conducting preclinical studies and clinical trials necessary to obtain regulatory approval is costly and time consuming. We may never succeed in achieving regulatory approval for any of our product candidates. The probability of success for each product candidate will be affected by numerous factors, including preclinical 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 for our clinical development programs can vary significantly for each current and future product candidate 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 will need to raise substantial additional capital in the future to complete clinical development for 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 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.

General and administrative expenses

Our general and administrative expenses consist primarily of salaries, benefits, travel and stock-based compensation expense, and other related costs for our employees and consultants in executive, 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, and conducting commercial assessments for our product candidates.

We expect our general and administrative expenses to increase substantially as we hire additional personnel to support commercialization of our product candidates. We also anticipate increased expenses related to audit, legal, regulatory, and tax-related services associated with maintaining compliance with stock exchange listing

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and SEC requirements, director s and officer s liability insurance premiums, and investor relations-related expenses. Additionally, if and when we believe that a regulatory approval of a product candidate appears likely, we expect to incur significant increases in our general and administrative expenses relating to the sales and marketing of the product candidate.

Other (Expense) Income

Other (expense) income has included interest expense on our convertible notes payable, including amortization of debt discount, the change in fair value of the convertible preferred stock warrant liability, the change in fair value of the convertible preferred stock purchase right liability and interest income earned on cash and cash equivalents and short-term investments. The convertible preferred stock purchase right expired in June 2012, at which time the fair value of the convertible preferred stock purchase right liability was recognized in other (expense) income. In connection with the IPO, all of our outstanding warrants to purchase convertible preferred stock were either (i) exercised and the underlying shares of preferred stock were automatically converted into shares of common stock or (ii) converted into warrants to purchase common stock. Prior to the exercise and conversion of the warrants to purchase convertible preferred stock, we performed the final revaluation of the warrant liability upon the closing of the IPO in August 2014 and recorded the $2.6 million increase in fair value to change in fair value of convertible preferred stock warrant liability. The warrant liability was then reclassified to additional paid-in capital.

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 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.

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, 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 or state of consummation 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

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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, 2014, 2013 and 2012 there were no material adjustments to our prior period estimates of accrued expenses for clinical trials.

Convertible Preferred Stock Warrant Liability

Prior to our IPO, warrants exercisable for shares of our Series A and Series C convertible preferred stock were classified as liabilities at their estimated fair value, based on the characteristics and provisions of each instrument. At each reporting date the convertible preferred stock warrants were revalued, with fair value changes recorded as a component of other (expense) income.

Through December 31, 2012, we estimated the fair value of our outstanding convertible preferred stock warrants using a Black-Scholes-Merton option pricing model based on inputs as of the valuation measurement dates for the estimated fair value of the underlying convertible preferred stock, the remaining contractual terms of the warrants, the risk-free interest rate, the expected dividend yield and the estimated volatility of the price of our convertible preferred stock. In 2013, all of our outstanding convertible preferred stock warrants were valued using a hybrid of the option pricing model and the probability-weighted expected return method. The key inputs into the models included the probability and timing of expected liquidity event dates, discount rates and the selection of appropriate market comparable transactions and multiples to apply to our various historical and forecasted operating metrics.

In connection with the IPO, all of the outstanding warrants to purchase convertible preferred stock were either (i) exercised and the underlying shares of preferred stock were automatically converted into shares of common stock or (ii) converted into warrants to purchase common stock. Prior to the exercise and conversion of the warrants to purchase convertible preferred stock, we performed the final revaluation of the warrant liability upon the closing of the IPO in August 2014 and recorded the $2.6 million increase in fair value to change in fair value of convertible preferred stock warrant liability on the statement of operations. The warrant liability was then reclassified to additional paid-in capital.

Other Information

Net Operating Loss and Research and Development Tax Credit Carryforwards

As of December 31, 2014, we had federal and California net operating loss, or NOL, carryforwards of $60.5 million and $59.4 million, respectively. Our federal and California NOL carryforwards will begin to expire in 2030, unless we utilize them beforehand. As of December 31, 2014, we also had federal and California research and development tax credit carryforwards of $2.8 million and $1.6 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 Internal Revenue Code, or IRC, 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 the closing of this offering or

subsequent 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, 2014, we had a full valuation allowance against our deferred tax assets.

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JOBS Act

On April 5, 2012, the Jumpstart Our Business Startups Act of 2012, or 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.

We are in the process of evaluating the benefits of relying on other exemptions and reduced reporting requirements provided by the JOBS Act. Subject to certain conditions set forth in the JOBS Act, as an emerging growth company, we intend to rely on certain of these exemptions, 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 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 IPO.

Results of Operations

Comparison of the Years Ended December 31, 2014 and 2013

The following table sets forth the significant components of our results of operations for the years ended December 31, 2014 and 2013 (in thousands):

	Years Ended December 31,		
	2014	2013	Change
Research and development	$ 31,803	$ 16,336	$ 15,467
General and administrative	7,836	3,514	4,322
Interest expense	39	2,528	(2,489)
Change in fair value of convertible preferred stock warrant liability	3,300	(2,833)	6,133

Research and development expenses. The increase of $15.5 million in research and development expenses was primarily due to a $7.3 million increase in ongoing clinical trial-related expenses for our OTO-104 product candidate that advanced into a Phase 2b clinical trial at the end of 2013 and a $4.8 million increase in clinical trial-related expenses for our AuriPro product candidate that advanced into Phase 3 clinical trials during the second half of 2013. In addition, there was a $2.4 million increase in personnel costs, including stock-based compensation expense and overhead, due to additional headcount, $2.0 million in expenses associated with OTO-311 following our acquisition in October 2013 of certain assets and rights to intellectual property related to OTO-311, and a $0.3 million increase in lab supplies and services to support our increased research and development activities. These increases were partially

offset by a $1.3 million decrease in license fees, which was primarily due to two clinical milestones achieved during 2013, compared with no such clinical milestones achieved during 2014.

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General and administrative expenses. The increase of $4.3 million in general and administrative expenses was primarily related to the expansion of our operating activities, costs associated with becoming a publicly traded company, and costs related to commercial preparation activities. The overall increase is comprised of an increase of $2.2 million in personnel costs, including stock-based compensation expense, due to additional headcount, and an increase of $2.1 million in expenses for outside services, including consulting costs, legal fees, accounting fees, corporate development and market research.

Interest expense. During the year ended December 31, 2014, our interest expense consisted of amortization of the deferred financing costs on our credit facility with Square 1 Bank, which expired on July 31, 2014. During the year ended December 31, 2013, our interest expense was comprised of non-cash interest expense, including amortization of debt discount, on the convertible notes that we issued between August 2012 and January 2013, which were all converted into shares of our convertible preferred stock in August 2013. The decrease of $2.5 million in interest expense was a result of the convertible notes being outstanding during most of the year ended December 31, 2013 but not during the year ended December 31, 2014.

Change in fair value of convertible preferred stock warrant liability. The fair value of our convertible preferred stock warrant liability increased by $3.3 million for the year ended December 31, 2014 compared to a decrease of $2.8 million for the year ended December 31, 2013. These changes resulted from the revaluation of our convertible preferred stock warrants.

In connection with the IPO, all of our outstanding warrants to purchase convertible preferred stock were either (i) exercised and the underlying shares of preferred stock were automatically converted into shares of common stock or (ii) converted into warrants to purchase common stock. Prior to the exercise and conversion of the warrants to purchase convertible preferred stock, we performed the final revaluation of the warrant liability upon the closing of the IPO in August 2014 and recorded the $2.6 million increase in fair value to change in fair value of convertible preferred stock warrant liability. The warrant liability was then reclassified to additional paid-in capital.

Comparison of the Years Ended December 31, 2013 and 2012

The following table sets forth the significant components of our results of operations for the years ended December 31, 2013 and 2012 (in thousands):

	Years Ended December 31,		
	2013	2012	Change
Research and development	$ 16,336	$ 8,523	$ 7,813
General and administrative	3,514	2,408	1,106
Interest expense	2,528	444	2,084
Change in fair value of convertible preferred stock warrant liability	(2,833)	(100)	(2,733)
Change in fair value of convertible preferred stock purchase right		(3,707)	3,707

Research and development expenses. The increase of $7.8 million in research and development expenses was primarily due to a $3.3 million increase in clinical trial-related expenses for our AuriPro product candidate that advanced into Phase 3 clinical trials during the second half of 2013, a $2.2 million increase in clinical trial-related expenses for our OTO-104 product candidate that advanced into a Phase 2b clinical trial at the end of 2013 and a $1.1 million increase in license fees we paid to the University of California following our achievement of success-based

clinical milestones in 2013 for AuriPro and OTO-104. In addition, there was a $1.0 million increase in payroll, allocated overhead and travel expenses during 2013 due to an increase in the number of development personnel and $0.2 million in expenses associated with our acquisition in October 2013 of certain assets and rights to intellectual property related to OTO-311.

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General and administrative expenses. The increase of $1.1 million in general and administrative expenses was due to a $0.5 million increase in expenses for outside services that were primarily related to market research and preparing for our initial public offering, a $0.3 million increase in intellectual property expenses, a $0.2 million increase in personnel costs related to additional headcount, including stock-based compensation expense, and $0.1 million of legal expenses associated with our acquisition in October 2013 of certain assets and rights to intellectual property related to OTO-311.

Interest expense. Interest expense during the years ended December 31, 2013 and 2012 was comprised of non-cash interest expense on the convertible notes that we issued between August 2012 and January 2013, which were all converted into shares of our preferred stock in August 2013. The increase of $2.1 million in interest expense was due to the acceleration of debt discount of $1.1 million resulting from the conversion of the convertible notes prior to the end of their terms and an increase of $1.0 million due to higher convertible note balances that were outstanding during approximately eight months during 2013 compared to approximately four months during 2012.

Change in fair value of convertible preferred stock warrant liability. The fair value of our convertible preferred stock warrant liability decreased by $2.8 million for the year ended December 31, 2013 compared to a decrease of $0.1 million for the year ended December 31, 2012. The decreases resulted from the revaluation of our convertible preferred stock warrants.

Change in fair value of preferred stock purchase right. The $3.7 million decrease in the fair value of our convertible preferred stock purchase right liability for the year ended December 31, 2013 compared to the year ended December 31, 2012 was due to the expiration of our convertible preferred stock purchase right in June 2012.

Liquidity and Capital Resources

We have incurred significant losses and negative cash flows from operations since our inception. As of December 31, 2014, we had an accumulated deficit of $102.5 million and we expect to continue to incur significant losses for the foreseeable future. We expect our research and development and general and administrative expenses to continue to increase substantially for the foreseeable future and, as a result, we will 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.

From inception to December 31, 2014, we have raised net cash proceeds of approximately $143.8 million from the sale of convertible preferred stock, convertible notes and warrants. In August 2014, we completed our IPO in which we sold 7,187,500 shares of common stock at an offering price of $16.00 per share, which included the exercise in full by the underwriters of their option to purchase up to 937,500 additional shares of common stock. Proceeds from the IPO were approximately $104.1 million, net of underwriting discounts, commissions and offering-related transaction costs incurred. As of December 31, 2014, we had cash, cash equivalents and short-term investments of $156.0 million.

In January 2015, we completed a follow-on public offering of 2,932,500 shares of our common stock, which includes the exercise in full by the underwriters of their option to purchase 382,500 shares of common stock, at an offering price of $29.25 per share. Proceeds from the follow-on public offering were approximately $80.0 million, net of underwriting discounts, commissions and offering-related transaction costs.

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The following table summarizes our cash flows for the years ended December 31, 2014, 2013 and 2012 (in thousands):

	Years Ended December 31,		
	2014	2013	2012
Net cash (used in) provided by:			
Operating activities	$ (35,219)	$ (19,467)	$ (10,828)
Investing activities	(16,931)	(511)	(185)
Financing activities	154,676	52,599	8,014
Net increase (decrease) in cash	102,526	32,621	(2,999)

Operating activities. For all years presented, the primary use of cash was to fund increased levels of development activities for our product candidates, which activities and uses of cash we expect to continue for the foreseeable future. During the year ended December 31, 2014, we used cash in operating activities of $35.2 million, while our net loss was $42.9 million. The difference consisted of $5.2 million of net non-cash adjustments, primarily comprised of stock-based compensation expense, the change in fair value of our convertible preferred stock warrant liability and depreciation and amortization expense, together with $2.5 million of net change in our operating assets and liabilities.

During the year ended December 31, 2013, we used cash in operating activities of $19.5 million, while our net loss was $19.6 million. The difference consisted of $0.1 million of net non-cash adjustments, primarily comprised of stock-based compensation expense, the change in fair value of our convertible preferred stock warrant liability, depreciation and amortization expense and non-cash interest expense.

During the year ended December 31, 2012, we used cash in operating activities of $10.8 million, while our net loss was $7.6 million. The difference consisted of $2.6 million of net non-cash adjustments, primarily comprised of a $3.7 million gain on the change in fair value of the convertible preferred stock purchase right which expired in 2012, partially offset by non-cash adjustments for stock-based compensation expense, depreciation and amortization expense, non-cash interest expense and deferred rent, together with $0.6 million of net change in our operating assets and liabilities.

Investing activities. Net cash used in investing activities was $16.9 million, $0.5 million and $0.2 million for the years ended December 31, 2014, 2013 and 2012, respectively. During the year ended December 31, 2014, $16.2 million was used to purchase short-term investments, $0.8 million was used for capital expenditures and $0.1 million was provided by the removal of the restriction on our restricted cash. Net cash used in investing activities during the years ended December 31, 2013 and 2012 was primarily for capital expenditures.

Financing activities. Net cash provided by financing activities was $154.7 million, $52.6 million and $8.0 million for the years ended December 31, 2014, 2013 and 2012, respectively. During 2014, proceeds from our IPO were $104.1 million after deducting underwriting discounts, commissions and offering-related transaction costs, net proceeds from the sale of our series D convertible preferred stock were $49.2 million and proceeds from the cash exercise of convertible preferred stock warrants were $1.2 million. During 2013, net proceeds from the sale of our series C convertible preferred stock were $45.6 million and net proceeds from the issuance of convertible notes were $7.0 million. During 2012, net proceeds from our issuance of convertible notes were $8.0 million.

Funding Requirements

To date, we have not generated any revenue. We do not expect to generate any revenue from any product candidates that we develop unless and until we obtain regulatory approval and commercialize our products or enter into collaborative agreements with third parties. In the future, if AuriPro is approved for commercial sale in the United States, we may generate revenue from product sales. We do not expect to commercialize AuriPro

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before 2016, if ever. We expect to continue to incur significant losses for the foreseeable future, and we expect the losses to increase as we continue the development of, and seek regulatory approvals for, our product candidates, and begin to commercialize any approved products. 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 expect to incur additional costs associated with operating as a public company and we will need substantial additional funding in connection with our continuing operations.

We believe that our existing cash and cash equivalents and short-term investments, together with the proceeds from our follow-on public offering completed in January 2015, will be sufficient to fund our projected operating requirements for at least the next 24 months. However, we may need to raise additional funds sooner to prepare for the commercialization of AuriPro and the further development of our other product candidates and may not be able to do so on commercially reasonable terms, or at all.

Until we can generate a sufficient amount of revenue from our products, if ever, we expect to finance our future cash needs through public or private equity or debt financings, or other sources such as potential collaboration agreements. In any event, we do not expect to achieve significant revenue from product sales prior to the use of our existing cash balance. Additional capital may not be available on reasonable terms, if 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 design, initiation, progress, size, timing, costs and results of preclinical studies and clinical trials for our product candidates;
- 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, preclinical studies and, if approved, for commercial sale;

the cost of establishing 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;

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the cost of preparing, filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;

our need to expand our development activities, including our need and ability to hire 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, 2014 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)		
Operating lease obligations[1]	$ 552	$ 731	$ 7	$	$ 1,290
Total contractual obligations	$ 552	$ 731	$ 7	$	$ 1,290

(1) We lease our facility under an operating lease. In September 2011, we entered into a non-cancelable lease for laboratory and office space that commenced in February 2012 and expires in February 2017. Minimum future annual obligations under this lease total $1.0 million, and are reflected in the table above.

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, 2014, we were unable to estimate the timing or likelihood of achieving the milestones or making future product sales and, therefore, any related payments are not included in the table above. Under our license agreement with UC, we are obligated to pay annual license maintenance fees of $25,000 until we commercialize the

first product covered under the license agreement.

Item 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Fluctuations

As of December 31, 2014, we had cash and cash equivalents and short-term investments of $156.0 million which are comprised of cash in checking and savings accounts, money market funds and certificates of deposit. 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.

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Foreign Currency Exchange Rate Fluctuations

To date, the vast majority of our contractual obligations have been denominated in U.S. dollars; however, we contract with a CRO in the United Kingdom and are subject to fluctuation in foreign currency rates in connection with such contract. In the future, we may contract with investigational sites and other CROs 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 contract.

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

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Otonomy, Inc.

Index to Financial Statements

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Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Otonomy, Inc.

We have audited the accompanying balance sheets of Otonomy, Inc. as of December 31, 2014 and 2013, and the related statements of operations and comprehensive loss, convertible preferred stock and stockholders equity (deficit) and cash flows for each of the three years in the period ended December 31, 2014. These financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company s internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, 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. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Otonomy, Inc. at December 31, 2014 and 2013, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2014, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

San Diego, California

March 18, 2015

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Otonomy, Inc.

Balance Sheets

(in thousands, except share and per share data)

	December 31, 2014	December 31, 2013
Assets		
Current assets:		
Cash and cash equivalents	$ 139,810	$ 37,284
Restricted cash		75
Short-term investments	16,223	
Prepaid and other current assets	1,669	1,654
Total current assets	157,702	39,013
Property and equipment, net	1,257	683
Other long-term assets	205	61
Total assets	$ 159,164	$ 39,757
Liabilities, Convertible Preferred Stock and Stockholders Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 1,710	$ 2,014
Accrued expenses	3,046	384
Accrued compensation	575	244
Current portion of deferred rent	86	73
Total current liabilities	5,417	2,715
Convertible preferred stock warrant liability		646
Deferred rent, net of current portion	134	220
Total liabilities	5,551	3,581
Commitments and Contingencies		
Convertible preferred stock, $0.001 par value; no shares authorized at December 31, 2014; 9,519,809 shares authorized at December 31, 2013		
Series A convertible preferred stock, no shares issued or outstanding at December 31, 2014; 404,671 shares designated at December 31, 2013; 339,863 shares issued and outstanding at December 31, 2013; $2,987 liquidation preference at December 31, 2013		10,561
Series B convertible preferred stock, no shares issued or outstanding at December 31, 2014; 1,708,076 shares designated at December 31, 2013; 1,708,076 shares issued and outstanding at December 31, 2013; $15,014 liquidation preference at December 31, 2013		23,007
Series C convertible preferred stock, no shares issued or outstanding at December 31, 2014; 7,407,062 shares designated at December 31, 2013; 7,040,026 shares issued and		61,585

outstanding at December 31, 2013; $92,823 liquidation preference at December 31, 2013		
Stockholders equity (deficit):		
Preferred stock, $0.001 par value, 10,000,000 shares authorized at December 31, 2014; no shares authorized at December 31, 2013; no shares issued or outstanding at December 31, 2014 and 2013		
Common stock, $0.001 par value; 200,000,000 and 11,851,717 shares authorized at December 31, 2014 and 2013, respectively; 21,173,270 and 75,325 shares issued and outstanding as of December 31, 2014 and 2013, respectively	21	
Additional paid-in capital	256,061	580
Accumulated deficit	(102,469)	(59,557)
Total stockholders equity (deficit)	153,613	(58,977)
Total liabilities, convertible preferred stock, and stockholders equity (deficit)	$ 159,164	$ 39,757

See accompanying notes.

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Otonomy, Inc.

Statements of Operations and Comprehensive Loss

(in thousands, except share and per share data)

	Years Ended December 31,		
	2014	2013	2012
Operating expenses:			
Research and development	$ 31,803	$ 16,336	$ 8,523
General and administrative	7,836	3,514	2,408
Total operating expenses	39,639	19,850	10,931
Loss from operations	(39,639)	(19,850)	(10,931)
Other (expense) income:			
Interest expense	(39)	(2,528)	(444)
Change in fair value of convertible preferred stock warrant liability	(3,300)	2,833	100
Change in fair value of convertible preferred stock purchase right			3,707
Other income (expense), net	101	(14)	(1)
Total other (expense) income	(3,238)	291	3,362
Net loss and comprehensive loss	(42,877)	(19,559)	(7,569)
Accretion to redemption value of convertible preferred stock	(35)	(539)	(801)
Net loss attributable to common stockholders	$ (42,912)	$ (20,098)	$ (8,370)
Net loss per share attributable to common stockholders, basic and diluted	$ (5.46)	$ (268.79)	$ (118.99)
Weighted-average shares used to compute net loss per share attributable to common stockholders, basic and diluted	7,853,228	74,772	70,343

See accompanying notes.

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Otonomy, Inc.

Statements of Convertible Preferred Stock and Stockholders Equity (Deficit)

(in thousands, except share data)

Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Series C Convertible Preferred Stock		Series D Convertible Preferred Stock		Common Stock		Additional Paid-in	A m
ares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Capital	D
9,863	$ 10,556	1,708,076	$ 21,690		$		$	72,631	$	$ 198	$
								1,066		3	
										191	
	3		798								
9,863	10,559	1,708,076	22,488					73,697		392	
				7,040,026	61,567						

								1,628		5
										183
	2		519		18					
9,863	10,561	1,708,076	23,007	7,040,026	61,585			75,325		580
						4,126,080	49,239			
								61,974		110
								228,902		1,201
9,863)	(10,561)	(1,708,076)	(23,007)	(7,040,026)	(61,616)	(4,126,080)	(49,243)	13,619,569	14	144,413
								7,187,500	7	104,119
										3,946
										1,692

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$	$	$	$ 21,173,270	$ 21	$ 256,061	$ (

See accompanying notes.

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Otonomy, Inc.,

Statements of Cash Flows

(in thousands)

	Years Ended December 31,		
	2014	**2013**	**2012**
Cash flows from operating activities:			
Net loss	$ (42,877)	$ (19,559)	$ (7,569)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	213	257	192
Stock-based compensation	1,692	183	191
Non-cash interest expense	39	2,528	444
Change in fair value of convertible preferred stock warrant liability	3,300	(2,833)	(100)
Change in fair value of convertible preferred stock purchase right			(3,707)
Amortization of discount or premium on short-term investments	1		
Deferred rent	(73)	(24)	317
Changes in operating assets and liabilities:			
Prepaid and other assets	(34)	(1,013)	(530)
Accounts payable	(309)	874	641
Accrued expenses	2,498	60	(472)
Accrued compensation	331	60	(235)
Net cash used in operating activities	(35,219)	(19,467)	(10,828)
Cash flows from investing activities:			
Purchases of short-term investments	(16,224)		
Decrease (increase) in restricted cash	75	(25)	
Purchases of property and equipment	(782)	(486)	(185)
Net cash used in investing activities	(16,931)	(511)	(185)
Cash flows from financing activities:			
Proceeds from convertible notes payable		7,009	8,011
Proceeds from issuance of convertible preferred stock, net of issuance costs	49,239	45,585	
Proceeds from issuance of common stock, net of fees	104,126		
Proceeds from issuance of restricted common stock and exercise of stock options, net of early exercise liability	110	5	3
Proceeds from exercise of preferred stock warrants	1,201		
Net cash provided by financing activities	154,676	52,599	8,014
Net change in cash	102,526	32,621	(2,999)
Cash and cash equivalents at beginning of period	37,284	4,663	7,662

Cash and cash equivalents at end of period	$ 139,810	$ 37,284	$ 4,663
Supplemental disclosure of non-cash investing and financing activities:			
Purchase of property and equipment in accounts payable and accrued expenses	$ 5	$ 15	$
Conversion of convertible notes payable and accrued interest into convertible preferred stock	$	$ 15,982	$
Deferred public offering costs in accrued expenses	$ 164	$	$

See accompanying notes.

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Otonomy, Inc.,

Notes to Financial Statements

1. Description of Business and Basis of Presentation

Description of Business

Otonomy, Inc. (the Company) was incorporated in the state of Delaware on May 6, 2008. The Company is a clinical-stage biopharmaceutical company focused on the development and commercialization of innovative therapeutics for the treatment of diseases and disorders of the ear. The Company s proprietary technology is designed to deliver drug that is retained in the ear for an extended period of time following a single local administration. Utilizing this technology, the Company has advanced three product candidates into development. AuriPro™ is a sustained-exposure formulation of the antibiotic ciprofloxacin for which the Company has completed two Phase 3 clinical trials in pediatric patients with middle ear effusion at the time of tympanostomy tube placement surgery. The Company submitted a New Drug Application for AuriPro to the U.S. Food and Drug Administration in February 2015. OTO-104 is a sustained-exposure formulation of the steroid dexamethasone that is in a Phase 2b clinical trial for the treatment of patients with Ménière s disease. OTO-311 is a sustained-exposure formulation of the N-methyl-D-aspartate (NMDA) receptor antagonist gacyclidine in preclinical development as a potential treatment for tinnitus.

Initial Public Offering

In August 2014, the Company completed its initial public offering (the IPO) of 7,187,500 shares of common stock, which includes the exercise in full by the underwriters of their option to purchase up to 937,500 shares of common stock, at an offering price of $16.00 per share. Proceeds from the IPO were $104.1 million, net of underwriting discounts and commissions and offering-related transaction costs incurred. In connection with the IPO: (i) the Company s outstanding shares of convertible preferred stock were automatically converted into 13,619,569 shares of common stock, (ii) the warrants exercisable for Series A convertible preferred stock were automatically converted into warrants exercisable for 142,113 shares of common stock and (iii) the warrants exercisable for Series C convertible preferred stock were exercised and such shares were automatically converted into 228,902 shares of common stock.

Reverse Stock Split

On July 31, 2014, the Company filed an amendment to its amended and restated certificate of incorporation, affecting a one-for-35.16 reverse stock split of its outstanding common and convertible preferred stock, which was approved by the Company s board of directors on July 29, 2014. The accompanying financial statements and notes to the financial statements give retroactive effect to the reverse split for all periods presented.

Basis of Presentation

As of December 31, 2014, the Company has devoted substantially all of its efforts to product development, raising capital, and building infrastructure and has not realized revenues from its planned principal operations. The accompanying 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, 2014, the Company had cash, cash equivalents and short-term investments of $156.0 million and an accumulated deficit of $102.5 million. The Company anticipates that it will continue to incur net losses into the

foreseeable future as it: (i) continues the development and begins commercialization of its product candidates AuriPro, OTO-104 and OTO-311; (ii) works to develop additional product candidates through research and development programs; and (iii) expands its corporate infrastructure. The Company plans to continue to fund its losses from operations and capital funding needs through future debt and/or equity

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financings or other sources, such as potential collaboration agreements. If the Company is not able to secure adequate additional funding, 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 accompanying financial statements have been prepared in accordance with 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. The most significant estimates in the Company s financial statements relate to equity awards and clinical trial accruals. Although these estimates are based on the Company s knowledge of current events and 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 and Cash Equivalents

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.

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 (see Note 7). 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.

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Fair Value of Financial Instruments

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

Property and Equipment

Property and equipment generally consist of manufacturing equipment, furniture and fixtures, computers, and scientific and office equipment and are recorded at cost and depreciated using the straight-line method over the estimated useful lives of the assets (generally three 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 and, accordingly, has not recognized any impairment losses through December 31, 2014.

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. The Company makes estimates of accrued expenses as of each balance sheet date based on the facts and circumstances known at that time. Accordingly, the Company s clinical trial accruals are dependent upon accurate reporting by contract research organizations and other third-party vendors. Although the Company does not expect its estimates to be materially different from amounts actually incurred, the Company s 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, 2014, 2013 and 2012, there were no material adjustments to prior period estimates of accrued expenses for clinical trials.

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.

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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 general and administrative expenses in the accompanying statements of operations.

Convertible Preferred Stock

Prior to the Company s IPO, the Company s outstanding convertible preferred stock was classified as temporary equity instead of stockholders deficit in accordance with authoritative guidance for the classification and measurement of potentially redeemable securities, as the stock was conditionally redeemable at the holder s option and upon certain change in control events that are outside the Company s control, including the liquidation, sale, or transfer of control of the Company. Upon such change in control events, holders of the convertible preferred stock could cause its redemption.

In connection with the IPO, all of the Company s outstanding shares of convertible preferred stock were automatically converted into shares of common stock.

Convertible Preferred Stock Warrants

Prior to the Company s IPO, warrants exercisable for shares of the Company s Series A and Series C convertible preferred stock were classified as liabilities in the accompanying balance sheets based upon the characteristics and provisions of each instrument. Convertible preferred stock warrants were classified as derivative liabilities and were recorded at their fair value on the date of issuance. At each reporting date the convertible preferred stock warrants were revalued, with fair value changes recognized as increases in or decreases to the change in fair value of convertible preferred stock warrant liability in the accompanying statements of operations.

In connection with the IPO, all of the Company s outstanding warrants to purchase convertible preferred stock were either (i) exercised and the underlying shares of preferred stock were automatically converted into shares of common stock or (ii) converted into warrants to purchase common stock. Prior to the exercise and conversion of the warrants to purchase convertible preferred stock, the Company performed the final revaluation of the warrant liability upon the closing of the IPO in August 2014 and recorded the $2.6 million increase in fair value to change in fair value of convertible preferred stock warrant liability in the accompanying statements of operations. The warrant liability was then reclassified to additional paid-in capital on the accompanying balance sheets.

Convertible Preferred Stock Purchase Right

The Company determined that its obligation to issue, and the investors obligation to purchase, additional shares of the Company s Series B convertible preferred stock represented a freestanding financial instrument and required liability accounting. This freestanding convertible preferred stock purchase right liability was initially recorded at fair value, with fair value changes recognized as increases in or decreases to the change in fair value of convertible preferred stock purchase right in the accompanying statements of operations. In June 2012, the convertible preferred stock purchase right expired and its change in fair value was recognized in change in fair value of convertible preferred stock purchase right in the accompanying 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

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option pricing model net of estimated forfeitures. For awards subject to time-based vesting conditions, stock-based compensation expense is recognized using the straight-line method.

The Company accounts for stock options granted to non-employees, including members of the scientific advisory board, using the fair value approach. Stock options granted to non-employees are subject to periodic revaluation over their vesting terms with the related expense being recognized as research and development and/or general and administrative expense in the accompanying statements of operations.

Income Taxes

The Company accounts for income taxes under the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements. Under this method, deferred tax assets and liabilities are determined on the basis of the differences between the financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in income in the period that includes the enactment date.

The Company recognizes net deferred tax assets to the extent that the Company believes these assets are more likely than not to be realized. In making such a determination, management considers all available positive and negative evidence, including future reversals of existing taxable temporary differences, projected future taxable income, tax-planning strategies, and results of recent operations. If management determines that the Company would be able to realize its deferred tax assets in the future in excess of their net recorded amount, management would make an adjustment to the deferred tax asset valuation allowance, which would reduce the provision for income taxes.

The Company uses a two-step approach to recognizing and measuring uncertain tax positions. The first step is to evaluate tax positions taken or expected to be taken in a tax return by assessing whether they are more likely than not sustainable, based solely on their technical merits, upon examination and including resolution of any related appeals or litigation process. The second step is to measure the associated tax benefit of each position as the largest amount that the Company believes is more likely than not realizable. Differences between the amount of tax benefits taken or expected to be taken in the Company s income tax returns and the amount of tax benefits recognized in its financial statements, represent its unrecognized income tax benefits, which the Company either records as a liability or as a reduction of deferred tax assets.

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. For all periods presented, comprehensive loss is equal to net loss.

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.

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Potentially dilutive securities excluded from the calculation of diluted net loss per share attributable to common stockholders are as follows (in common stock equivalent shares):

	As of December 31,		
	2014	2013	2012
Convertible preferred stock		9,493,489	2,453,463
Convertible notes payable			580,580
Warrants to purchase convertible preferred stock		483,517	255,013
Warrants to purchase common stock	142,113		
Unvested restricted common stock subject to repurchase	13,627		859
Options to purchase common stock	2,707,477	1,235,705	382,663
	2,863,217	11,212,711	3,672,578

Recently Issued Accounting Standards

In June 2014, the Financial Accounting Standards Board (FASB) issued guidance that eliminates the financial reporting distinction between development stage entities and other reporting entities under accounting principles generally accepted in the United States of America (GAAP), thereby eliminating the requirements to present inception-to-date information in the financial statements and to label the financial statements as those of a development stage entity. The Company has early adopted, as permitted, the new guidance as of June 30, 2014, and therefore has not labeled its financial statements as those of a development stage entity or included any inception-to-date information. The new guidance is to be applied retrospectively and impacts the presentation of the financial statements, but does not impact the Company s financial position, results of operations or cash flows.

In August 2014, the FASB issued guidance which requires management to assess an entity s ability to continue as a going concern and to provide related footnote disclosure in certain circumstances. This standard is effective for annual reporting periods ending after December 15, 2016 and interim periods thereafter. Early application is permitted. The adoption of this guidance will have no impact on the Company s financial position, results of operations or cash flows.

3. Available-for-Sale Securities

The Company invests in available-for-sale securities consisting of money market funds and certificates of deposit. 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 $18.8 million as of December 31, 2014. 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 $16.2 million as of December 31, 2014. There have been no unrealized gains or losses related to the Company s short-term investments.

The Company determined that there were no other-than-temporary declines in the value of any available-for-sale securities as of December 31, 2014. The Company did not hold any available-for-sale securities as of December 31, 2013. All of 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 the custodian bank or from a professional pricing service. The fair values of available-for-sale securities are validated by comparing the fair values reported by the custodian bank to quoted market prices or to fair values obtained from a second source professional pricing service.

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4. Balance Sheet Details

Prepaid and Other Current Assets

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

	December 31,	
	2014	2013
Prepaid clinical trial costs	$ 843	$ 1,478
Other	826	176
Total	$ 1,669	$ 1,654

Property and Equipment, Net

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

	December 31,	
	2014	2013
Laboratory equipment	$ 1,109	$ 908
Manufacturing equipment	945	392
Computer equipment and software	116	93
Leasehold improvements	67	67
Office furniture	19	17
	2,256	1,477
Less: accumulated depreciation and amortization	(999)	(794)
Total	$ 1,257	$ 683

Depreciation expense was $0.2 million, $0.3 million and $0.2 million for the years ended December 31, 2014, 2013 and 2012, respectively.

Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31,	
	2014	2013
Accrued clinical trial costs	$ 2,397	$ 196
Accrued other	649	188

Total	$ 3,046	$ 384

5. Notes Payable and Convertible Preferred Stock Warrants

Notes Payable

In August 2012 and October 2012, the Company entered into a note and warrant purchase agreement (the 2012 Convertible Note Agreement) under which the Company issued $8.0 million in secured convertible promissory notes (the 2012 Notes) with a stated interest rate of 8% per annum. In January 2013, the Company issued an additional $7.0 million in secured convertible promissory notes in a subsequent closing under the 2012 Convertible Note Agreement (the 2013 Notes).

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In connection with the issuance of the 2012 Notes and the 2013 Notes, the Company issued warrants which were exercisable for Series C convertible preferred stock. The debt discount was amortized using the effective interest rate method over the term of the convertible notes to interest expense in the accompanying statements of operations.

In August 2013, the 2012 Notes and the 2013 Notes in the amount of approximately $16.0 million, including interest, converted into 1,818,191 shares of Series C convertible preferred stock. Concurrent with the closing of the Series C convertible preferred stock, the warrants issued in conjunction with the 2012 Notes and the 2013 Notes converted into warrants for the purchase of an aggregate of 341,404 shares of Series C convertible preferred stock with an exercise price of $8.79 per share.

Warrants

Outstanding warrants as of December 31, 2013 consisted of warrants to purchase 64,801 shares of Series A convertible preferred stock at an exercise price of $31.092 and warrants to purchase 341,404 shares of Series C convertible preferred stock at an exercise price $8.79 per share. The aggregate fair value of the Series A and Series C convertible preferred stock warrants as of December 31, 2013 was approximately $46,000 and $0.6 million, respectively. The shares of Series A convertible preferred stock were convertible into shares of common stock at a ratio of 1:2.193204365. The shares of Series C convertible preferred stock were convertible into shares of common stock at a ratio of 1:1.

In connection with the closing of the IPO, (i) the Series A convertible preferred stock warrants automatically converted into warrants to purchase 142,113 shares of common stock at an exercise price of $14.1765 per share, which warrants remained outstanding as of December 31, 2014, and (ii) of the 341,404 Series C convertible preferred stock warrants, 204,773 warrants were net exercised for 92,271 shares of Series C convertible preferred stock, the remaining warrants for the purchase of 136,631 shares of Series C convertible preferred stock were cash exercised for proceeds to the Company of $1.2 million, and all of the shares of Series C convertible preferred stock were automatically converted to shares of common stock.

Non-Cash Interest Expense

The following table summarizes interest expense recognized under the Company s convertible notes payable and convertible preferred stock warrants (in thousands):

	Years Ended December 31,		
	2014	**2013**	**2012**
Stated interest on convertible notes payable	$	$ 749	$ 228
Amortization of deferred financing costs associated with the convertible preferred stock warrants	39	1,779	216
Total interest expense	$ 39	$ 2,528	$ 444

6. Commitments and Contingencies

Operating Leases

In December 2010, the Company signed a sublease agreement with a related party for a one-year term through December 31, 2011. In December 2011, the Company extended the term of the sublease through December 2012 on a month-to-month basis. In June 2012, the Company vacated the premises and fulfilled its obligations under the sublease.

In September 2011, the Company entered into a lease agreement with a third party on a new facility for a five-year term commencing in February 2012.

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Rent expense was $0.4 million for each of the years ended December 31, 2014, 2013 and 2012, 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 accompanying balance sheets.

As of December 31, 2014, future minimum annual obligations under all non-cancellable operating lease commitments, including the facility lease described above are as follows (in thousands):

2015	$ 552
2016	571
2017	160
2018	7
Total	$ 1,290

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, 2014 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.

License Agreements

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,		
	2014	**2013**	**2012**
License and other fees	$ 75	$ 250	$ 25
Milestone fees		1,100	
Total license and related fees	$ 75	$ 1,350	$ 25

Intellectual Property Licenses

The Company has acquired exclusive rights to develop patented rights, information rights and related know-how for the Company s AuriPro, OTO-104 and OTO-311 product candidates and potential future product candidates under licensing agreements with third parties in the course of its research and development activities. The licensing rights obligate the Company to make payments to the licensors for license fees, milestones, license maintenance fees and royalties. Annual license and maintenance fees related to these agreements is $25,000. The license and maintenance fees will continue until the first commercial sale of a product. In addition, the Company issued 710 shares of common stock as compensation for one of the licenses. The Company is also responsible for patent prosecution costs, in the

event such costs are incurred.

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Under one of these agreements, the Company has achieved five development milestones, totaling $1.2 million, related to its clinical trials for both AuriPro and OTO-104. The Company may be obligated to make additional milestone payments under these agreements as follows (in thousands, except share data):

	Shares of Common Stock	Cash Payments
Development	1,066	$ 3,235
Regulatory	1,066	12,670
Commercialization		1,000
Total	2,132	$ 16,905

In addition, the Company may owe royalties of less than five percent on sales of commercial products, if any, developed using these licensed technologies. The Company may also be obligated to pay to the licensors a percentage of fees received if and when the Company sublicenses the technology. As of December 31, 2014, the Company has not yet developed a commercial product using the licensed technologies and it has not entered into any sublicense agreements for the technologies.

Other Royalty Arrangements

The Company entered into an agreement related to three provisional patents for AuriPro under which the Company may be obligated to pay a one-time milestone payment of $0.5 million upon the first commercial sale of an approved product and to pay royalties of less than one percent on product sales. 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 AuriPro; or (ii) 10 years after the first commercial sale of AuriPro after receipt of regulatory approval for AuriPro in such country.

During October 2014, the Company entered into an exclusive license agreement with Ipsen that enables the Company to use clinical and non-clinical gacyclidine data generated by Ipsen to support worldwide development and regulatory filings for OTO-311. Under this license agreement, the Company is obligated to pay Ipsen low single-digit royalties on annual net sales of OTO-311 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.

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The following fair value hierarchy table presents the Company s assets and liabilities measured at fair value on a recurring basis as of December 31, 2014 and 2013 (in thousands):

	Fair Value Measurement at Reporting Date Using			
	Total	Level 1	Level 2	Level 3
December 31, 2014:				
Assets				
Money market funds	$ 17,840	$ 17,840	$	$
Certificates of deposit	17,160		17,160	
	$ 35,000	$ 17,840	$ 17,160	$