Otonomy, Inc.
Form S-1
January 08, 2015
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As filed with the Securities and Exchange Commission on January 8, 2015.

Registration No. 333-

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-1

REGISTRATION STATEMENT

Under

The Securities Act of 1933

OTONOMY, INC.

(Exact name of Registrant as specified in its charter)

Delaware	**2834**	**26-2590070**
(State or other jurisdiction of incorporation or organization)	**(Primary Standard Industrial Classification Code Number)**	**(I.R.S. Employer Identification Number)**

6275 Nancy Ridge Drive, Suite 100

San Diego, California 92121

(858) 242-5200

(Address, including zip code, and telephone number, including area code, of Registrant s principal executive offices)

David A. Weber, Ph.D.

President and Chief Executive Officer

Otonomy, Inc.

6275 Nancy Ridge Drive, Suite 100

San Diego, California 92121

(858) 242-5200

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Kenneth A. Clark **Tony Jeffries** **Daniel R. Koeppen** **Wilson Sonsini Goodrich & Rosati, P.C.** **650 Page Mill Road** **Palo Alto, California 94304** **(650) 493-9300**	**Paul E. Cayer** **Chief Financial and Business Officer** **Otonomy, Inc.** **6275 Nancy Ridge Drive, Suite 100** **San Diego, California 92121** **(858) 242-5200**	**Charles S. Kim** **Andrew S. Williamson** **David G. Peinsipp** **Cooley LLP** **4401 Eastgate Mall** **San Diego, California 92121** **(858) 550-6000**

Approximate date of commencement of proposed sale to the public: As soon as practicable after this registration statement becomes effective.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 check the following box: ¨

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If this Form is a post effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If this Form is a post effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

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

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

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Proposed Maximum Aggregate Offering Price(1)	Amount of Registration Fee(2)
Common Stock, $0.001 par value	$86,250,000	$10,023

(1) Estimated solely for the purpose of calculating the amount of the registration fee in accordance with Rule 457(o) under the Securities Act of 1933, as amended. Includes the offering price of any additional shares that the underwriters have the option to purchase.
(2) Calculated pursuant to Rule 457(o) under the Securities Act of 1933, as amended, based on an estimate of the proposed maximum aggregate offering price.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

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The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED JANUARY 8, 2015

PRELIMINARY PROSPECTUS

Shares

Common Stock

We are selling shares of our common stock.

Our common stock is listed on The NASDAQ Global Select Market under the symbol OTIC. On January 7, 2015, the last reported sale price of our common stock on The NASDAQ Global Select Market was $33.79 per share.

We are an emerging growth company as defined under the federal securities laws and, as such, have elected to comply with certain reduced public company reporting requirements.

	Per Share	Total
Public offering price	$	$
Underwriting discounts and commissions[(1)]	$	$
Proceeds to Otonomy, Inc., before expenses	$	$

(1) See Underwriting for a description of the compensation payable to the underwriters.
We have granted the underwriters an option for a period of 30 days to purchase up to an additional shares from us at the public offering price, less the underwriting discounts and commissions.

Investing in our common stock involves risks. See Risk Factors beginning on page 12 to read about factors you should consider before buying shares of our common stock.

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares of common stock to purchasers on or about , 2015.

J.P. Morgan

Piper Jaffray **Cowen and Company**

Sanford C. Bernstein

, 2015

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Neither we nor the underwriters have authorized anyone to provide any information or to make any representations other than those contained in this prospectus or in any free writing prospectuses we have prepared. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus is current only as of its date.

For investors outside the United States: Neither we nor any of the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about, and to observe any restrictions relating to, this offering and the distribution of this prospectus.

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PROSPECTUS SUMMARY

This summary highlights selected information appearing elsewhere in this prospectus and is qualified in its entirety by the more detailed information and financial statements included elsewhere in this prospectus. This summary may not contain all the information you should consider before investing in our common stock. You should carefully read this prospectus in its entirety before investing in our common stock, including the sections titled Risk Factors and Management s Discussion and Analysis of Financial Condition and Results of Operations and our financial statements and related notes included elsewhere in this prospectus. Unless the context otherwise requires, we use the terms Otonomy, the Company, we, us and our in this prospectus to refer to Otonomy, Inc.

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 plan to submit a New Drug Application, or NDA, for AuriPro to the FDA in the first quarter of 2015. If approved within the 12 month standard review period, we anticipate a commercial launch for AuriPro in the United States in the first half 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 as a 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. Our mission is to develop and commercialize novel and best-in-class therapeutics to address unmet medical needs in the emerging otology market.

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

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 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.

Overview of Otology and Current Treatments

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 include the outer, middle and inner ear. The outer ear is the 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. The middle ear is the cavity on the inner-side of the ear drum containing the three small bones that transmit sound to the inner ear. Infection or inflammation in this area, known as otitis media, is a common occurrence in young children. The inner ear is the 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.

Outer ear infections 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 recurrence of infection in some patients.

Middle ear infections 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. 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.

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Inner ear disorders 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 drug to the middle ear cavity through the ear drum, and then to the inner ear compartment via passage through the round window membrane. 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. This limits inner ear drug exposure, which likely reduces the therapeutic effect and increases treatment variability across patients.

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.

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 Product Candidates

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. AuriPro has been formulated to provide sustained-exposure of ciprofloxacin so that a single administration provides a full course of treatment. 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. Moreover, current ear drop products require multi-dose, multi-day regimens for efficacy. Full compliance with these regimens can be challenging, and missed antibiotic doses can compromise efficacy and increase the potential for bacterial resistance.

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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. A p-value is the probability that the reported result was achieved purely by chance, such that a p-value of less than or equal to 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. 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 plan to submit an NDA for AuriPro to the FDA in the first quarter of 2015. If approved within the 12 month standard review period, we anticipate a commercial launch for AuriPro in the United States in the first half of 2016.

The initial target market for AuriPro totals approximately one million TTP procedures conducted each year in the United States, for which antibiotic ear drops are routinely used off-label today. In addition, 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. We have global commercialization rights to AuriPro with patent protection in the United States until at least 2030.

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

We have completed a randomized, prospective, double-blind, placebo-controlled, multicenter, 44-patient Phase 1b clinical trial of a single IT injection of OTO-104 in patients with Ménière s disease. Results demonstrated that OTO-104 is well tolerated when administered as a single IT injection and 12 mg of OTO-104 was associated with clinically meaningful improvements in both vertigo frequency and tinnitus compared to placebo three months after treatment. There were no serious adverse events observed during the clinical trial. 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 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.

The initial target market for OTO-104 is the more than 600,000 patients diagnosed with Ménière s disease in the United States. In addition, 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. We have global commercialization rights to OTO-104 with patent protection in the United States until at least 2029.

OTO-311: Sustained-Exposure Treatment for Tinnitus

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. Tinnitus is often described as a ringing in the ear but can also sound like roaring, clicking, hissing or buzzing. People with severe tinnitus may have trouble hearing, working and sleeping. At this time, there is no cure for tinnitus and there are no FDA-approved drugs for treating this debilitating condition.

Historic and emerging clinical data provide support for the use of NMDA receptor antagonists, including gacyclidine, for the treatment of tinnitus. Mechanistically, agents from this therapeutic class may act to reduce dysfunctional activity resulting from injury to the hearing organ, or cochlea, and be perceived by the patient as tinnitus. For example, Phase 2 clinical trials with several agents have demonstrated reductions in the severity of tinnitus and improvement in the functional status of treated patients. We expect that the results of these trials will be instructive in the design and implementation of our clinical development program. The goal of our 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. 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.

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;

Develop OTO-104 for treatment of Ménière s disease and other inner ear disorders;

Establish our own sales and marketing capabilities to commercialize our products in the United States;

Maximize the commercial potential of our products outside the United States; and

Utilize our technology and our broad patent portfolio to develop OTO-311 and expand our product pipeline.

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Founders and Management Team

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 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.

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 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.

Updates and Recent Developments

NDA Submission for AuriPro. We are preparing an NDA for AuriPro, which incorporates feedback received from a pre-NDA meeting and communications with the FDA. We plan to submit the NDA to the FDA during the first quarter of 2015. If approved within the 12 month standard review period, we anticipate product introduction in the United States during the first half of 2016.

Phase 2b results for OTO-104 in Ménière s disease patients. We completed enrollment in our Phase 2b clinical trial for OTO-104 in Ménière s disease patients in December 2014, exceeding the target enrollment of 140 patients with a final total of 154 patients. This trial is expected to serve as one of two pivotal, single-dose efficacy trials required to support U.S. regulatory approval. We expect to report results from this clinical trial in the second quarter of 2015 and, if results are positive, to initiate a second pivotal trial of OTO-104 in 2015.

Initiation of a clinical trial for AuriPro in one or more additional indications. Potential expansion indications for AuriPro include 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. We plan to initiate clinical trials for AuriPro in one or more of these indications during the first half of 2015.

IND filing and start of Phase 1 clinical trial for OTO-311. 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.

Cash and short-term investments balance. We had cash and short-term investments totaling $156.0 million on December 31, 2014 compared to $165.2 million on September 30, 2014.

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Risks Associated with Our Business

Our business is subject to numerous risks that you should consider before investing in us. These risks are described more fully in the section titled Risk Factors immediately following this prospectus summary. These risks include, among others:

- 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 currently have no source of product revenue and may never become profitable;
- We will require substantial additional financing to commercialize our lead product candidate, AuriPro, and to obtain regulatory approval for OTO-104 and OTO-311;
- We are substantially dependent on the regulatory and commercial success of AuriPro;
- We are also dependent upon the clinical, regulatory, and commercial success of OTO-104, our second product candidate;
- In addition to AuriPro and OTO-104, our long-term prospects are dependent in part on advancing other product candidates, such as OTO-311, into clinical development and through to regulatory approval and commercialization;
- 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;
- 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;
- Even if our product candidates obtain regulatory approval, they may fail to achieve the broad degree of market acceptance and use necessary for commercial success;
- To establish our sales and marketing infrastructure, we will need to increase the size of our organization, and we may experience difficulties in managing this growth. If we are unable to establish sales and marketing

capabilities, we will be unable to successfully commercialize our products, if approved, or generate product revenue;

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

Our product candidates, if approved, will face significant competition in the biopharmaceutical market 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.

Corporate and Other Information

Our principal executive offices are located at 6275 Nancy Ridge, Suite 100, San Diego, California 92121, and our telephone number is (858) 242-5200. Our website is www.otonomy.com. Information contained on, or that can be accessed through, our website is not incorporated by reference into this prospectus, and you should not consider information on our website to be part of this prospectus. We were incorporated in Delaware in May 2008.

Otonomy, the Otonomy logo and other trademarks or service marks of Otonomy appearing in this prospectus are the property of Otonomy. Trade names, trademarks and service marks of other companies appearing in this prospectus are the property of their respective holders. We have omitted the ® and designations, as applicable, for the trademarks used in this prospectus.

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We are an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act. We will remain an emerging growth company until the earliest to occur of: the last day of the fiscal year in which we have more than $1.0 billion in annual revenue; the date we qualify as a large accelerated filer, with at least $700 million of equity securities held by non-affiliates; the issuance, in any three-year period, by us of more than $1.0 billion in non-convertible debt securities; and the last day of the fiscal year ending after the fifth anniversary of our initial public offering, or December 31, 2019. As a result of this status, we have taken advantage of reduced reporting requirements in this prospectus. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. 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.

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The Offering

Common stock offered by us	shares
Common stock to be outstanding after this offering	shares
Option to purchase additional shares	We have granted the underwriters an option, exercisable for 30 days after the date of this prospectus, to purchase up to an additional shares of common stock from us.
Use of proceeds	We intend to use the net proceeds from this offering to fund expenses in connection with obtaining the regulatory approval and commercializing AuriPro in the United States, if approved, and conducting clinical trials for AuriPro in one or more potential expansion indications; OTO-104 clinical development, including completion of the OTO-104 Phase 2b clinical trial and, if results are positive, initiation and completion of a Phase 3 clinical trial, and initiation and completion of one or more open-label, multiple-dose safety studies in Ménière s patients; preclinical development and a Phase 1 clinical trial for OTO-311; and for research and development activities, working capital, facilities expansion and other general corporate purposes. See Use of Proceeds.
NASDAQ Global Select Market trading symbol	OTIC

The number of shares of our common stock to be outstanding after this offering is based on 21,172,221 shares of common stock outstanding as of September 30, 2014, and excludes:

2,058,910 shares of common stock issuable upon the exercise of options outstanding as of September 30, 2014, at a weighted-average exercise price of $3.51 per share;

142,113 shares of common stock issuable upon the exercise of outstanding warrants to purchase shares of common stock as of September 30, 2014, at an exercise price of $14.1765 per share of common stock subject to such warrants;

2,602,675 shares of common stock reserved for future issuance under our 2014 Equity Incentive Plan, or our 2014 Plan, and any additional shares that become available under our 2014 Plan pursuant to provisions thereof that automatically increase the share reserve under the plan each year, as more fully described in the section titled Executive Compensation Employee Benefit and Stock Plans; and

380,000 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan, or ESPP, and any additional shares that become available under our ESPP pursuant to provisions thereof that automatically increase the share reserve under the plan each year, as more fully described in the

section titled Executive Compensation Employee Benefit and Stock Plans.

Unless otherwise noted, the information in this prospectus reflects and assumes no exercise of outstanding options or warrants to purchase common stock after September 30, 2014, and the underwriters do not exercise their option to purchase up to an additional shares of our common stock in this offering.

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Summary Financial Data

The following tables summarize our summary financial data for the periods and as of the dates indicated. We have derived our summary statements of operations data for each of the years ended December 31, 2012 and 2013 from our audited financial statements and related notes included elsewhere in this prospectus. We have derived our summary statements of operations data for each of the nine months ended September 30, 2013 and 2014 and the summary balance sheet data as of September 30, 2014 from our unaudited financial statements and related notes included elsewhere in this prospectus. Our interim unaudited financial statements have been prepared in accordance with generally accepted accounting principles in the United States of America on the same basis as the annual audited financial statements and, in the opinion of management, reflect all adjustments, consisting only of normal recurring adjustments, necessary for the fair statement of our financial position as of September 30, 2014 and our results of our operations for the nine months ended September 30, 2013 and 2014. Our historical results are not necessarily indicative of the results that may be expected in the future, and our unaudited interim results are not necessarily indicative of the results that may be expected for the full year or any other period. You should read this information together with our financial statements and related notes appearing elsewhere in this prospectus and the information in the sections titled Selected Financial Data and Management s Discussion and Analysis of Financial Condition and Results of Operations.

	Years Ended December 31,		Nine Months Ended September 30,	
	2012	2013	2013	2014
	(in thousands, except share and per share data)		(unaudited)	
Statements of Operations Data:				
Operating expenses:				
Research and development	$ 8,523	$ 16,336	$ 9,698	$ 24,616
General and administrative	2,408	3,514	2,284	5,169
Total operating expenses	10,931	19,850	11,982	29,785
Loss from operations	(10,931)	(19,850)	(11,982)	(29,785)
Other income (expense)	3,362	291	180	(3,298)
Net loss and comprehensive loss	(7,569)	(19,559)	(11,802)	(33,083)
Accretion to redemption value of convertible preferred stock	(801)	(539)	(526)	(35)
Net loss attributable to common stockholders	$ (8,370)	$ (20,098)	$ (12,328)	$ (33,118)
Net loss per share attributable to common stockholders, basic and diluted[(1)]	$ (118.99)	$ (268.79)	$ (165.29)	$ (9.83)
Weighted-average shares used to compute net loss per share attributable to common stockholders, basic and diluted[(1)]	70,343	74,772	74,585	3,369,437

(1) See Note 2 to our financial statements included elsewhere in this prospectus for an explanation of the methods used to calculate the historical net loss per share attributable to common stockholders, basic and diluted, and the number of shares used in the calculations of these per share amounts.

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	As of September 30, 2014	
	Actual	As Adjusted[1][2]
	(in thousands) (unaudited)	
Balance Sheet Data:		
Cash	$ 165,155	$
Working capital	161,761	
Total assets	168,325	
Accumulated deficit	(92,675)	
Total stockholders equity	162,598	

(1) The as adjusted balance sheet data in the table above reflects the sale of shares of our common stock in this offering and the application of the net proceeds at an assumed public offering price of $ per share, which was the last sale price of our common stock as reported by The NASDAQ Global Select Market on , 2015, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

(2) Each $1.00 increase (decrease) in the assumed public offering price of $ per share would increase (decrease) each of cash, working capital, total assets and total stockholders equity by approximately $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each increase (decrease) of 1.0 million shares in the number of shares of common stock offered by us would increase (decrease) each of cash, working capital, total assets and total stockholders equity by approximately $ million, assuming that the assumed public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. The as adjusted information discussed above is illustrative only and will be adjusted based on the actual public offering price and other terms of this offering determined at pricing.

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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 prospectus, including our financial statements, the notes thereto and the section titled Management s Discussion and Analysis of Financial Condition and Results of Operations, before you decide to purchase shares of our common stock. 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 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 $7.6 million, $19.6 million and $33.1 million for the years ended December 31, 2012 and 2013 and for the nine months ended September 30, 2014, respectively. As of September 30, 2014, we had an accumulated deficit of $92.7 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 September 30, 2014, we had a cash balance of

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$165.2 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;
- 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.

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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;
- 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.

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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 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;
- 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

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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.

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;

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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 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,

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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;
- 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

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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;
- 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 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.

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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.

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.

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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.

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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.

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 September 30, 2014, we had 38 full-time employees, including 30 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

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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.

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.

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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 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;

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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 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.

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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.

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 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.

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

The strength of patents in the pharmaceutical field involves complex legal and scientific questions and can be uncertain. This uncertainty includes changes to the patent laws through either legislative action to change statutory patent law or court action that may reinterpret existing law or rules in ways affecting the scope or validity of issued patents. The patent applications that we own or in-license may fail to result in issued patents in the United States or foreign countries with claims that cover our product 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 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.

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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 provide 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 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.

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.

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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.

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.

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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.

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.

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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 submitted an application or 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;

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

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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 intend to seek 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 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.

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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;
- 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.

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.

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 this Offering and Our Common Stock

The market price of our common stock has been and may continue to be volatile, and you may not be able to sell your shares at or above the offering price.

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.

We and the underwriters will determine the offering price of our common stock through negotiation. This price will not necessarily reflect the price at which investors in the market will be willing to buy and sell our shares following

this offering. 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. As a result of this volatility, investors may not be able to sell their common stock at or above the offering price. The market price of our common stock following our initial public offering has been and is likely to continue to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including:

- regulatory or legal developments;

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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;

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 following this offering, the market price of our common stock could decline significantly.

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As of September 30, 2014, we had 21,172,221 shares of common stock outstanding, approximately 13,984,721 of which are subject to 180-day lock-up agreements entered into in connection with our initial public offering that expire on February 8, 2015. Following the expiration of the lock-ups (or earlier if permitted by the managing underwriters), all shares of our common stock, other than shares subject to 90-day lock-up agreements entered into in connection with this offering, 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. See Shares Eligible for Future Sale for additional information. In addition, shares issued or issuable upon exercise of warrants vested as of the expiration of the applicable 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 September 30, 2014, options to purchase 910,005 shares of our common stock were exercisable.

Certain holders of approximately 14,079,588 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 180-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.

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.

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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.

New investors in our common stock will experience immediate and substantial dilution after this offering.

If you purchase shares of our common stock in this offering, you will experience substantial and immediate dilution of $ per share in the as adjusted net tangible book value per share of our common stock as of September 30, 2014, based on the difference between an assumed public offering price of $ per share, which was the last reported sales price of our common stock on The NASDAQ Global Select Market on , 2015, and the as adjusted net tangible book value per share of our common stock as of September 30, 2014, because the price that you pay will be substantially greater than our net tangible book value per share of the common stock that you acquire. This dilution is due in large part to the fact that our earlier investors paid substantially less than the public offering price when they purchased their shares of our capital stock. You will experience additional dilution upon exercise of warrants to purchase common stock, upon exercise of options to purchase common stock under our equity incentive plans, if we issue restricted stock to our employees under our equity incentive plan, or if we otherwise issue additional shares of our common stock. For a further description of the dilution that you will experience immediately after this offering, see Dilution.

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 after this offering may effectively limit the voting power of other stockholders, including purchasers in this offering.

Upon the closing of this offering, our executive officers, directors and current beneficial owners of 5% or more of our common stock will, in aggregate, beneficially own approximately % of our outstanding common stock, assuming exercise of the underwriters option to purchase additional shares. 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

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you and other stockholders. For example, our board of directors has the authority to issue up to 10,000,000 shares of preferred stock. Our board of directors can fix the price, rights, preferences, privileges, and restrictions of the preferred stock without any further vote or action by our stockholders. The issuance of shares of preferred stock may delay or prevent a change in control transaction. As a result, the market price of our common stock and the voting and other rights of our stockholders may be adversely affected. An issuance of shares of preferred stock may result in the loss of voting control to other stockholders.

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

- establish that our board of directors is divided into three classes, Class I, Class II and Class III, with each class serving staggered three year terms;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- provide that our directors may only be removed for cause;
- eliminate cumulative voting in the election of directors;
- authorize our board of directors to issues shares of preferred stock and determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval;
- provide our board of directors with the exclusive right to elect a director to fill a vacancy or newly created directorship;
- permit stockholders to only take actions at a duly called annual or special meeting and not by written consent;
- prohibit stockholders from calling a special meeting of stockholders;
- require that stockholders give advance notice to nominate directors or submit proposals for consideration at stockholder meetings;
- authorize our board of directors, by a majority vote, to amend the bylaws; and

require the affirmative vote of at least 66 2/3% or more of the outstanding shares of common stock to amend many of the provisions described above.

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

We will have broad discretion in the use of proceeds from this offering and our existing cash, and may invest or spend the proceeds in ways with which you do not agree and in ways that may not yield a return.

We will have broad discretion in the application of the net proceeds from this offering and our existing cash. You may not agree with our decisions, and our use of the proceeds and our existing cash may not improve our results of operation or enhance the value of our common stock. Though we currently intend to use approximately $78.0 million to fund our planned registration, commercialization and potential indication expansion of AuriPro in the United States, if approved, approximately $50.0 million to fund the costs of the clinical development of OTO-104, approximately

$15.0 million to fund the costs of preclinical development and a Phase 1 clinical trial for OTO-311, and the remainder for the research and development activities, working capital, facilities expansion and other general corporate purposes, we cannot specify with certainty all of the particular uses of the net proceeds that we will receive from this offering and our existing cash, or the amounts that we will actually spend on the uses set forth above. The amounts and timing of our actual expenditures will depend on numerous factors, including the ongoing status of and results from clinical trials and other studies, the product approval process with the FDA, and the scope of our commercialization efforts, as well as any strategic collaborations that we may enter into with third parties for our product candidates, any unforeseen cash needs, and our investments and acquisitions. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in using these proceeds. In addition, we may also use a portion of our net proceeds to acquire and invest in complementary products or businesses; however, we currently have no agreements or commitments to complete any such transaction. Investors will be relying on our judgment regarding the use of the net proceeds from this offering. You will not have the opportunity to influence our management s decisions on how to use the net proceeds from this offering. Our failure to apply the net proceeds of this offering effectively could result in financial losses that could materially impair our ability to pursue our strategy, cause the market price of our common stock to decline, or require us to raise additional capital.

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, 2013 we had U.S. federal and California net operating loss carryforwards, or NOLs, of approximately $46.8 million and $46.6 million, respectively, which expire in various years beginning in 2030, if not utilized. As of December 31, 2013, we had federal and California research and development tax credit carryforwards of approximately $1.6 million and $1.1 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 this offering or 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.

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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 Securities and Exchange Commission, or 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 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, 2013 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

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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.

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.

We have taken advantage of reduced reporting requirements in this prospectus. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. 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.

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The industry- and market-related estimates included in this prospectus are based on various assumptions and may prove to be inaccurate.

Industry- and market-related estimates included in this prospectus, including, without limitation, estimates related to our market size and industry data, are subject to uncertainty and are based on assumptions which may not prove to be accurate. This may have negative consequences, such as us overestimating our potential market opportunity. For more information, see the section titled Market, Industry and Other Data.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements generally relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- our expectations regarding our clinical development of OTO-104;
- 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 planned submission of an NDA for approval of AuriPro and 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;

developments and projections relating to our competitors and our industry;

our expectations regarding the expansion of our facilities;

our anticipated use of proceeds from this offering; and

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our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act.

In some cases, you can identify these statements by terms such as anticipate, believe, could, estimate, expects, may, plan, potential, predict, project, should, will, would or the negative of those terms, and similar exp convey uncertainty of future events or outcomes. These forward-looking statements reflect our beliefs and views with respect to future events and are based on estimates and assumptions as of the date of this prospectus and are subject to risks and uncertainties. We discuss many of these risks in greater detail in the section entitled Risk Factors. Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible 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. Given these uncertainties, you should not place undue reliance on these forward-looking statements.

You should carefully read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in this prospectus by these cautionary statements.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in any forward-looking statements, whether as a result of new information, future events or otherwise.

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MARKET, INDUSTRY AND OTHER DATA

We obtained the industry, market and similar data set forth in this prospectus from our own internal estimates and research, and from industry publications and research, primary market research commissioned by us, and surveys and studies conducted by third parties, such as the American Academy of Otolaryngology-Head and Neck Surgeons, the National Institute on Deafness and other Communications Disorders, and the American Tinnitus Association. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such information and estimates.

Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

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USE OF PROCEEDS

We estimate that the net proceeds to us from the sale of shares of our common stock in this offering will be $ million, based on an assumed public offering price of $ per share, which was the last sale price of our common stock as reported by The NASDAQ Global Select Market on , 2015, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, we estimate that our net proceeds would be $ million, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Each $1.00 increase or decrease in the assumed public offering price of $ per share would increase or decrease the net proceeds that we receive from this offering by approximately $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase or decrease of 1.0 million shares in the number of shares of common stock offered by us, as set forth on the cover page of this prospectus, would increase or decrease the net proceeds that we receive from this offering by approximately $ million, assuming that the assumed public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The principal purposes of this offering are to obtain additional capital to support our operations. More specifically, we anticipate that we will use the net proceeds from this offering, together with our existing cash, as follows:

- approximately $78.0 million to fund expenses in connection with obtaining the regulatory approval and commercializing AuriPro in the United States, if approved, and conducting clinical trials for AuriPro in one or more potential expansion indications;
- approximately $50.0 million to fund OTO-104 clinical development, including completion of the OTO-104 Phase 2b clinical trial and, if results are positive, initiation and completion of a Phase 3 clinical trial, and initiation and completion of one or more open-label, multiple-dose safety studies in Ménière s patients;
- approximately $15.0 million to fund preclinical development and a Phase 1 clinical trial for patients with tinnitus for OTO-311; and
- the remainder for research and development activities, working capital, facilities expansion and general corporate purposes.

We may also use a portion of the net proceeds from this offering and our existing cash to in-license, acquire or invest in complementary business, technologies, products or assets. However, we have no current plans, commitments or obligations to do so.

We believe that the net proceeds from this offering and our existing cash will be sufficient to fund our operations through at least the next 24 months. This expected use of the net proceeds from the offering represents our intentions based upon our current plans and business conditions. We cannot specify with certainty all of the particular uses of the net proceeds that we will receive from this offering, or the amounts that we will actually spend on the uses set forth above. The amounts and timing of our actual expenditures will depend on numerous factors, including the ongoing

status of and results from clinical trials and other studies, the product approval process with the FDA, and the scope of our commercialization efforts, as well as any strategic collaborations that we may enter into with third parties for our product candidates, any unforeseen cash needs, and our investments and acquisitions. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in using these proceeds. Investors will be relying on our judgment regarding the use of the net proceeds from this offering. Pending the use of proceeds as described above, we plan to invest the net proceeds that we receive in short-term and intermediate-term interest-bearing obligations, investment-grade investments, certificates of deposit or direct or guaranteed obligations of the U.S. government. We cannot predict whether the invested proceeds will yield a favorable return.

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MARKET PRICE OF OUR COMMON STOCK

Our common stock has been listed on The NASDAQ Global Select Market under the symbol OTIC since 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 intraday sales prices per share of our common stock, as reported on The NASDAQ Global Select Market:

2014	**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

2015	**High**	**Low**
First quarter ending March 31, 2015 (through January 7, 2015)	$35.05	$32.25

On January 7, 2015, the last reported sale price of our common stock on The NASDAQ Global Select Market was $33.79 per share. As of January 7, 2015, we had 74 holders 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.

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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.

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CAPITALIZATION

The following table sets forth our cash and capitalization as of September 30, 2014 on an actual basis and on an as adjusted basis to reflect our receipt of the net proceeds from our sale of shares of our common stock in this offering at an assumed public offering price of $ per share, which was the last sale price of our common stock as reported by The NASDAQ Global Select Market on , 2015, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

	As of September 30, 2014	
	Actual	As Adjusted[1]
	(in thousands, except share and per share data) (unaudited)	
Cash	$ 165,155	$
Stockholders Equity:		
Preferred stock, $0.001 par value: 10,000,000 shares authorized; no shares issued and outstanding, actual and as adjusted		
Common stock, $ 0.001 par value: 200,000,000 shares authorized; 21,172,221 shares issued and outstanding, actual; shares issued and outstanding, as adjusted	21	
Additional paid-in capital	255,252	
Accumulated deficit	(92,675)	
Total stockholders equity	162,598	
Total capitalization	$ 162,598	$

(1) Each $1.00 increase (decrease) in the assumed public offering price of $ per share, which was the last sale price of our common stock as reported by The NASDAQ Global Select Market on , 2015, would increase (decrease) each of cash, additional paid-in capital, total stockholders equity and total capitalization by approximately $ million, assuming that the number of shares of common stock offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each increase (decrease) of 1.0 million shares in the number of shares of common stock offered by us would increase (decrease) each of cash, additional paid-in capital, total stockholders equity and total capitalization by approximately $ million, assuming that the assumed public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. The as adjusted information discussed above is illustrative only and will be adjusted based on the actual public offering price and other terms of this offering determined at pricing.

The outstanding share information in the table above is based on 21,172,221 shares of common stock outstanding as of September 30, 2014, and excludes:

2,058,910 shares of common stock issuable upon the exercise of options outstanding as of September 30, 2014, at a weighted-average exercise price of $3.51 per share;

142,113 shares of common stock issuable upon the exercise of outstanding warrants to purchase shares of common stock as of September 30, 2014, at an exercise price of $14.1765 per share of common stock subject to such warrants;

2,602,675 shares of common stock reserved for future issuance under our 2014 Plan, and any additional shares that become available under our 2014 Plan pursuant to provisions thereof that automatically increase the share reserve under the plan each year; and

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380,000 shares of common stock reserved for future issuance under our ESPP, and any additional shares that become available under our ESPP pursuant to provisions thereof that automatically increase the share reserve under the plan each year.

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DILUTION

If you invest in our common stock, your ownership interest will be diluted to the extent of the difference between the amount per share paid by purchasers of shares of our common stock in this public offering and the as adjusted net tangible book value per share of our common stock immediately after completion of this offering.

Our net tangible book value is the amount of our total tangible assets less our total liabilities. Net tangible book value per share is our net tangible book value divided by the number of shares of common stock outstanding as of September 30, 2014. Our net tangible book value as of September 30, 2014 was $162.6 million, or $7.68 per share, based on the 21,172,221 shares of our common stock outstanding as of September 30, 2014.

After giving effect to the sale of shares of common stock in this offering at an assumed public offering price of $, which was the last sale price of our common stock as reported by The NASDAQ Global Select Market on , 2015, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value at September 30, 2014 would have been approximately $ million, or $ per share of common stock. This represents an immediate increase in as adjusted net tangible book value of $ per share to existing stockholders and an immediate dilution of $ per share to investors purchasing shares of common stock in this offering.

The following table illustrates this dilution on a per share basis:

Assumed public offering price per share		$
Net tangible book value per share as of September 30, 2014	$ 7.68	
Increase in net tangible book value per share attributable to investors participating in this offering		
As adjusted net tangible book value per share immediately after this offering		$
As adjusted dilution per share to investors participating in this offering		$

Each $1.00 increase (decrease) in the assumed public offering price of $ per share, which is the last sale price of our common stock as reported by The NASDAQ Global Select Market on , 2015, would increase (decrease) our as adjusted net tangible book value per share to investors participating in this offering by $, and would increase (decrease) dilution per share to investors participating in this offering by $, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, the as adjusted net tangible book value per share of our common stock after giving effect to this offering would be approximately $ per share, and the as adjusted dilution per share to investors participating in this offering would be approximately $ per share of common stock.

The number of shares of our common stock set forth in the table above excludes:

2,058,910 shares of common stock issuable upon the exercise of options outstanding as of September 30, 2014, at a weighted-average exercise price of $3.51 per share;

142,113 shares of common stock issuable upon the exercise of outstanding warrants to purchase shares of common stock as of September 30, 2014, at an exercise price of $14.1765 per share of common stock subject to such warrants;

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2,602,675 shares of common stock reserved for future issuance under our 2014 Plan and any additional shares that become available under our 2014 Plan pursuant to provisions thereof that automatically increase the share reserve under the plan each year; and

380,000 shares of common stock reserved for future issuance under our ESPP and any additional shares that become available under our ESPP pursuant to provisions thereof that automatically increase the share reserve under the plan each year.

Furthermore, we may choose to raise additional capital through the sale of equity or convertible debt securities due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent we issue additional shares of common stock or other equity or convertible debt securities in the future, there will be further dilution to investors participating in this offering.

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SELECTED FINANCIAL DATA

The following tables summarize our selected financial data for the periods and as of the dates indicated. We have derived our selected statements of operations data for each of the years ended December 31, 2012 and 2013, and our selected balance sheets data as of December 31, 2012 and 2013, from our audited financial statements and related notes included elsewhere in this prospectus. We have derived our selected statements of operations data for the nine months ended September 30, 2013 and 2014, and our selected balance sheet data as of September 30, 2014, from our unaudited financial statements and related notes included elsewhere in this prospectus. Our interim unaudited financial statements have been prepared in accordance with generally accepted accounting principles in the United States of America on the same basis as the annual audited financial statements and, in the opinion of management, reflect all adjustments, consisting only of normal recurring adjustments, necessary for the fair statement of our financial position as of September 30, 2014 and our results of our operations for the nine months ended September 30, 2013 and 2014. Our historical results are not necessarily indicative of the results that may be expected in the future, and our unaudited interim results are not necessarily indicative of the results that may be expected for the full year or any other period. You should read this information together with our financial statements and related notes appearing elsewhere in this prospectus and the information in the section titled Management s Discussion and Analysis of Financial Condition and Results of Operations.

	Years Ended December 31,		Nine Months Ended September 30,	
	2012	2013	2013	2014
	(in thousands, except share and per share data)		(unaudited)	
Statements of Operations Data:				
Operating expenses:				
Research and development	$ 8,523	$ 16,336	$ 9,698	$ 24,616
General and administrative	2,408	3,514	2,284	5,169
Total operating expenses	10,931	19,850	11,982	29,785
Loss from operations	(10,931)	(19,850)	(11,982)	(29,785)
Other income (expense)	3,362	291	180	(3,298)
Net loss and comprehensive loss	(7,569)	(19,559)	(11,802)	(33,083)
Accretion to redemption value of convertible preferred stock	(801)	(539)	(526)	(35)
Net loss attributable to common stockholders	$ (8,370)	$ (20,098)	$ (12,328)	$ (33,118)
Net loss per share attributable to common stockholders, basic and diluted[1]	$ (118.99)	$ (268.79)	$ (165.29)	$ (9.83)
Weighted-average shares used to compute net loss per share attributable to common stockholders, basic and diluted[1]	70,343	74,772	74,585	3,369,437

(1) See Note 2 to our financial statements included elsewhere in this prospectus for an explanation of the methods used to calculate the historical net loss per share attributable to common stockholders, basic and diluted, and the number of shares used in the calculations of these per share amounts.

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	As of December 31,		As of September 30,
	2012	2013	2014
		(in thousands)	(unaudited)
Balance Sheets Data:			
Cash	$ 4,663	$ 37,284	$ 165,155
Working capital	3,726	36,298	161,761
Total assets	5,904	39,757	168,325
Convertible notes payable, net	7,065		
Convertible preferred stock warrant liability	2,909	646	
Convertible preferred stock	33,047	95,153	
Accumulated deficit	(39,459)	(59,557)	(92,675)
Total stockholders (deficit) equity	(39,067)	(58,977)	162,598

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MANAGEMENT S DISCUSSION AND ANALYSIS OF

FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with Selected Financial Data and our financial statements and related notes included elsewhere in this prospectus. This discussion and analysis and other parts of this prospectus contain forward-looking statements based upon current beliefs, plans and expectations related to future events and our future financial performance that involve risks, uncertainties and assumptions, such as statements regarding our intentions, plans, objectives, expectations, forecasts and projections. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of several factors, including those set forth under Risk Factors and elsewhere in this prospectus. You should carefully read the Risk Factors section of this prospectus to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements. Please also see the section titled Special Note Regarding Forward-Looking Statements.

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 plan to submit a New Drug Application, or NDA, for AuriPro to the FDA in the first quarter of 2015. If approved within the 12 month standard review period, we anticipate a commercial launch for AuriPro in the United States in the first half 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 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.

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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 September 30, 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, which included $0.6 million of offering-related transaction costs incurred but not yet paid as of September 30, 2014. As of September 30, 2014, we had a cash balance of $165.2 million.

We have never been profitable, and as of September 30, 2014, we had an accumulated deficit of $92.7 million. Our net losses were $7.6 million and $19.6 million for the years ending December 31, 2012 and 2013, respectively, and $11.8 million and $33.1 million for the nine months ended September 30, 2013 and 2014, 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.

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.

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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. The expected net proceeds from this offering, together with our existing cash, 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 beyond the net proceeds from this offering. 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 the net proceeds from this offering and our existing cash balance 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 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.

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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. From our inception through September 30, 2014, we have incurred an aggregate of approximately $68.5 million of research and development expenses, the significant majority of which relate to our development of AuriPro and OTO-104.

The following table summarizes our research and development expenses (in thousands) by product candidate:

	Years Ended December 31,		Nine Months Ended September 30,	
	2012	2013	2013	2014
			(unaudited)	
Third-party development costs:				
AuriPro	$ 2,394	$ 5,712	$ 3,574	$ 9,815
OTO-104	1,290	3,510	1,744	8,135
OTO-311		46	10	567
Total third-party development costs	3,684	9,268	5,328	18,517
Other unallocated internal research and development costs	4,839	7,068	4,370	6,099
Total research and development expenses	$ 8,523	$ 16,336	$ 9,698	$ 24,616

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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

From our inception through September 30, 2014, we have incurred an aggregate of $20.0 million of 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,

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legal, regulatory, and tax-related services associated with maintaining compliance with stock exchange listing and SEC requirements, director s and officer s liability insurance premiums, and investor relations-related expenses. 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 Income (Expense)

Other income (expense) consists of 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. 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 income (expense). 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.

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 prospectus, 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

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, 2012 and 2013, and the nine months ended September 30, 2014, there were no material adjustments to our prior period estimates of accrued expenses for clinical trials.

Stock-Based Compensation

We measure our employee stock-based compensation expense at the grant date, based on the estimated fair value of the award, and recognize it as an expense, net of estimated forfeitures, over the requisite service period. We amortize stock-based compensation expense on a straight-line basis over the requisite service period for the entire award, which is generally four years; however, certain provisions in our equity incentive plan provide for shorter and longer vesting periods under certain circumstances.

We estimate the fair value of stock options and other equity-based compensation using a Black-Scholes-Merton option pricing model on the date of grant. The Black-Scholes-Merton option pricing model requires the input of subjective assumptions, including the risk-free interest rate, the expected dividend yield of our common stock, the expected volatility of the price of our common stock and the expected term of the option. These estimates involve inherent uncertainties and the application of management s judgment. If factors change and different assumptions are used, our stock-based compensation expense could be materially different in the future. See Note 8 to our financial statements included elsewhere in this prospectus for information concerning certain of the specific assumptions we used in applying the Black-Scholes-Merton option pricing model to determine the estimated fair value of our employee stock options granted in 2012 and 2013, and the nine months ended September 30, 2014.

Prior to our IPO in August 2014, the estimated fair value of the common stock underlying our stock options was determined at each grant date by our board of directors. To determine the fair value of our common stock underlying option grants our board of directors considered, among other things, input from management and contemporaneous valuations of our common stock prepared by an unrelated third-party valuation firm in accordance with the guidance provided by the American Institute of Certified Public Accountants 2004 Practice Aid, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. Our board of directors intended all options granted to be exercisable at a price per share not less than the per-share fair value of our common stock underlying those options on the date of grant. The per share common stock value was estimated by allocating the enterprise value using either the option pricing method or a hybrid of the option pricing method and probability-weighted expected return method.

In connection with our IPO, our common stock started trading on The NASDAQ Global Select Market. Consequently, after the IPO the fair value of the common stock underlying our stock options is the closing market price on the award grant date.

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 income (expense).

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

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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. 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, 2013, we had federal and California net operating loss, or NOL, carryforwards of $46.8 million and $46.6 million, respectively. Our federal and California NOL carryforwards will begin to expire in 2030, unless we utilize them beforehand. As of December 31, 2013, we also had federal and California research and development tax credit carryforwards of $1.6 million and $1.1 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 completed an IRC Section 382/383 analysis regarding the limitation of our NOL and R&D tax credit carryforwards as of December 31, 2013. As a result of the analysis, two ownership changes were determined to have occurred. 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, 2013, we had a full valuation allowance against our deferred tax assets.

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

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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 Nine Months Ended September 30, 2013 and 2014 (unaudited)

The following table sets forth the significant components of our results of operations for the nine months ended September 30, 2013 and 2014 (in thousands):

	Nine Months Ended September 30,		
	2013	2014	Change
	(unaudited)		
Research and development	$ 9,698	$ 24,616	$ 14,918
General and administrative	2,284	5,169	2,885
Interest expense	2,524	39	(2,485)
Change in fair value of convertible preferred stock warrant liability	(2,713)	3,300	6,013

Research and development expenses. Research and development expenses were $9.7 million and $24.6 million for the nine months ended September 30, 2013 and 2014, respectively. The increase of $14.9 million was primarily due to a $6.4 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 $6.2 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 $1.5 million increase in personnel costs, including stock-based compensation expense, due to additional headcount, $0.6 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 $0.2 million increase in lab supplies and services to support our increased research and development activities.

General and administrative expenses. General and administrative expenses were $2.3 million and $5.2 million for the nine months ended September 30, 2013 and 2014, respectively. The increase of $2.9 million 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 $1.5 million in expenses for outside services, including consulting costs, legal fees, accounting fees, corporate development and market research and an increase of $1.4 million in personnel costs, including stock-based compensation expense, due to additional headcount.

Interest expense. During the nine months ended September 30, 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

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outstanding during most of the nine months ended September 30, 2013 but not during the nine months ended September 30, 2014. During the nine months ended September 30, 2014, our interest expense consisted of the amortization of deferred financing costs on our credit facility with Square 1 Bank, which expired on July 31, 2014.

Change in fair value of convertible preferred stock warrant liability. The fair value of our convertible preferred stock warrant liability decreased by $2.7 million for the nine months ended September 30, 2013 compared to an increase of $3.3 million for the nine months ended September 30, 2014. 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.

Comparison of the Years Ended December 31, 2012 and 2013

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

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

Research and development expenses. Research and development expenses were $8.5 million and $16.3 million for the years ended December 31, 2012 and 2013, respectively. The increase of $7.8 million 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.

General and administrative expenses. General and administrative expenses were $2.4 million and $3.5 million for the years ended December 31, 2012 and 2013, respectively. The increase of $1.1 million 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 was $0.4 million and $2.5 million for the years ended December 31, 2012 and 2013, respectively. Our interest expense during these periods was comprised of non-cash interest expense on

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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 $0.1 million for the year ended December 31, 2012 compared to a decrease of $2.8 million for the year ended December 31, 2013. 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.

Quarterly Results of Operations

The following table sets forth selected unaudited quarterly statements of operations data for the last eleven fiscal quarters. The unaudited interim financial statements for each of these quarters have been prepared on the same basis as the audited consolidated financial statements included elsewhere in this prospectus and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary to a fair statement of our results of operations and financial position for these periods. This data should be read in conjunction with our audited consolidated financial statements and accompanying notes included elsewhere in this prospectus. The 2014 quarterly operating results are not necessarily indicative of our operating results for any future period.

	Three Months Ended										
	March 31, 2012	June 30, 2012	Sept. 30, 2012	Dec. 31, 2012	March 31, 2013	June 30, 2013	Sept. 30, 2013	Dec. 31, 2013	March 31, 2014	June 30, 2014	Sept. 30, 2014
	(unaudited, in thousands)										
Operating expenses:											
Research and development	$ 1,471	$ 1,294	$ 2,332	$ 3,426	$ 3,105	$ 3,045	$ 3,548	$ 6,638	$ 8,991	$ 8,264	$ 7,361
General and administrative	528	483	629	768	713	764	807	1,230	1,565	1,564	2,040
Total operating expenses	1,999	1,777	2,961	4,194	3,818	3,809	4,355	7,868	10,556	9,828	9,401
Loss from operations	(1,999)	(1,777)	(2,961)	(4,194)	(3,818)	(3,809)	(4,355)	(7,868)	(10,556)	(9,828)	(9,401)
Other income (expense):											
Interest expense			(119)	(325)	(485)	(561)	(1,478)	(4)	(4)	(4)	(31)
	27	29	22	22	1,816	708	189	120	(263)	(405)	(2,632)

Change in fair value of convertible preferred stock warrant liability											
Change in fair value of convertible preferred stock purchase right		3,707									
Other (expense) income, net	2	(1)	1	(3)	(2)	(4)	(3)	(5)	2	6	33
Total other income (expense)	29	3,735	(96)	(306)	1,329	143	(1,292)	111	(265)	(403)	(2,630)
Net loss and comprehensive loss	$ (1,970)	$ 1,958	$ (3,057)	$ (4,500)	$ (2,489)	$ (3,666)	$ (5,647)	$ (7,757)	$ (10,821)	$ (10,231)	$ (12,031)

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Liquidity and Capital Resources

We have incurred significant losses and negative cash flows from operations since our inception. As of September 30, 2014, we had an accumulated deficit of $92.7 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 September 30, 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, which included $0.6 million of offering-related transaction costs incurred but not yet paid as of September 30, 2014. As of September 30, 2014, we had a cash balance of $165.2 million.

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

	Years Ended December 31,		Nine Months Ended September 30,	
	2012	2013	2013	2014
			(unaudited)	
Net cash (used in) provided by:				
Operating activities	$ (10,828)	$ (19,467)	$ (11,141)	$ (27,021)
Investing activities	(185)	(511)	(445)	(327)
Financing activities	8,014	52,599	29,655	155,219
Net (decrease) increase in cash	(2,999)	32,621	18,069	127,871

Operating activities. Net cash used in operating activities was $10.8 million and $19.5 million for the years ended December 31, 2012 and 2013, respectively, and $11.1 million and $27.0 million for the nine months ended September 30, 2013 and 2014, respectively. For all periods 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.

Investing activities. Net cash used in investing activities was $0.2 million and $0.5 million for the years ended December 31, 2012 and 2013, respectively, and $0.4 million and $0.3 million for the nine months ended September 30, 2013 and 2014, respectively. Net cash used in investing activities in these periods was primarily for capital expenditures.

Financing activities. Net cash provided by financing activities was $8.0 million and $52.6 million for the years ended December 31, 2012 and 2013, respectively. During 2012, net proceeds from our issuance of convertible notes were $8.0 million. During 2013, net proceeds from our 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. Net cash provided by financing activities was $29.7 million and $155.2 million for the nine months ended September 30, 2013 and 2014, respectively. During the nine months ended September 30, 2013, net proceeds from our sale of our series C convertible preferred stock

were $22.6 million and net proceeds from the issuance of convertible notes were $7.0 million. During the nine months ended September 30, 2014, proceeds from our initial public offering were $104.7 million after deducting underwriting discounts, commissions and offering-related transaction costs paid (which excludes $0.6 million of offering-related transaction costs incurred but not yet paid as of September 30, 2014), 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.

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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 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 the net proceeds from this offering and our existing cash balance 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.

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 the net proceeds from this offering. 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;

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the number and characteristics of product candidates that we pursue;

the potential acquisition and in-licensing of other technologies, products or assets;

the extent to which we are required to pay milestone or other payments under our in-license agreements and the timing of such payments;

the cost of preparing, filing, prosecuting, 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, 2013 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]	$ 471	$ 960	$ 82	$	$ 1,513
Total contractual obligations	$ 471	$ 960	$ 82	$	$ 1,513

(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 $1.5 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, 2013, 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.

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Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Fluctuations

As of September 30, 2014, our cash balance consisted of cash of $165.2 million in checking and savings accounts. The primary objective of our investment activities is to preserve principal and liquidity while maximizing income without significantly increasing risk. We do not enter into investments for trading or speculative purposes. We do not believe that an immediate 10% increase in interest rates would have a material effect on the fair market value of our portfolio, and therefore, we do not expect our operating results or cash flows to be materially affected to any degree by a sudden change in market interest rates.

Foreign Currency Exchange Rate 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.

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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 plan to submit a New Drug Application, or NDA, for AuriPro to the FDA in the first quarter of 2015. If approved within the 12 month standard review period, we anticipate a commercial launch for AuriPro in the United States in the first half 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 plan to submit an NDA for AuriPro to the FDA in the first quarter of 2015. If approved within the 12 month standard review period, we anticipate a commercial launch for AuriPro in the United States in the first half 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 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.

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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 expect to submit an NDA seeking regulatory approval in the United States in the first quarter of 2015 and, if approved within the 12 month standard review period, anticipate a commercial launch in the first half 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 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 and pending patents 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.

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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.

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.

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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.

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.

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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:

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 ($p$ff£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 plan to submit an NDA for AuriPro to the FDA in the first quarter of 2015. If approved within the 12 month standard review period, we anticipate a commercial launch in the United States in the first half 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.

- 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

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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.

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 preliminary results that we believe are supportive of

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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 plan to submit an NDA for AuriPro to the FDA in the first quarter of 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.

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.

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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.

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

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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.

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.

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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.

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.

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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.

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 prospectus. 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.

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.

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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.

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.

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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.

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.

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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.

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.

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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.

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

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Risk Factors section of this prospectus. 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.

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 directed to the use of gacyclidine for the treatment of tinnitus. This patent has issued in the United States and is being prosecuted in several other jurisdictions. We also have our own patent 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.

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.

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.

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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.

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.

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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. Since 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 secondary 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.

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

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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.

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 two 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 pending 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.

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.

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 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

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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;

- 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;

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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 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.

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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, or twelve months from submission, 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.

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 patent expiration; or (4) the patent is invalid or will not be infringed upon by the manufacture, use or sale of the drug product for which the Section 505(b)(2) NDA is submitted. The last certification is known as a Paragraph IV certification. A notice of Paragraph IV certification must be provided to each owner of the patent that is the subject of the certification and to the holder of the approved NDA to which the Section 505(b)(2) NDA refers. If the NDA holder submits the patent information to the FDA prior to submission of the Section 505(b)(2) application and the NDA holder or patent owner(s) sues the Section 505(b)(2) applicant for infringement within 45 days of its receipt of the certification notice, the FDA is prevented from

approving that Section 505(b)(2) application until the earlier of 30 months from the receipt of the notice of the Paragraph IV certification, the expiration of the patent or such shorter or longer period as may be ordered by a court. This prohibition is

generally referred to as the 30-month stay. A Section 505(b)(2) applicant that is sued for infringement may file a counterclaim to challenge the listing of the patent or information submitted to FDA about the patent. If we file a Paragraph IV certification with any Section 505(b)(2) application, we cannot assure you that our application will not be significantly delayed as a result of costly patent litigation.

Post-Approval Requirements

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

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

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

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

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

product seizure or detention, or refusal to permit the import or export of products; or

injunctions or the imposition of civil or criminal penalties.

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.

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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 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 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.

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

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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 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

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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 $8.5 million and $16.3 million in research and development expenses in the years ended December 31, 2012 and 2013, respectively, and $24.6 million in research and development expenses for the nine months ended September 30, 2014. From our inception through September 30, 2014, we have incurred an aggregate of approximately $68.5 million of research and development expenses, the significant majority of which relate to our development of AuriPro and OTO-104.

Employees

As of September 30, 2014, we had 38 full-time employees, including 30 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.

Facilities

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.

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.

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MANAGEMENT

Executive Officers and Directors

The following table sets forth the names, ages and positions of our executive officers and directors as of December 31, 2014:

Name	Age	Position
David A. Weber, Ph.D.	55	President, Chief Executive Officer and Director
Paul E. Cayer	53	Chief Financial and Business Officer, and Secretary
Carl LeBel, Ph.D.	56	Chief Scientific Officer
Robert Michael Savel, II	47	Chief Technical Officer
Anthony J. Yost	56	Chief Commercial Officer
Non-Employee Directors		
Peter Bisgaard[2]	41	Chairman of the Board of Directors
Vickie Capps[1]	53	Director
Brian Dovey[3]	73	Director
Chau Q. Khuong[1][2][3]	38	Director
Jay Lichter, Ph.D.[1][2]	52	Director
John P. McKearn, Ph.D.[1]	61	Director
Heather Preston, M.D.[3]	48	Director

(1) Member of the audit committee
(2) Member of the compensation committee
(3) Member of the corporate governance and nominating committee

Executive Officers

David A. Weber, Ph.D. has served as our President and Chief Executive Officer and on our board of directors since November 2010. Prior to joining us, Dr. Weber served from February 2004 to April 2010 as the Chief Executive Officer of MacuSight, Inc., a developer of a sustained delivery formulation of sirolimus for the treatment of severe ophthalmic diseases. Prior to MacuSight, Dr. Weber served as acting Chief Executive Officer and Executive Vice President of Oculex Pharmaceuticals, Inc., a specialty pharmaceutical company focused on the development and commercialization of intraocular pharmaceuticals and drug delivery systems, until its acquisition by Allergan in 2003. Dr. Weber has also held management positions with Oral-B Laboratories, a developer and manufacturer of oral hygiene products, and with Procter & Gamble, Co., a consumer products company. Dr. Weber received his Ph.D. in medical microbiology from Creighton University and his Master s and Bachelor s degrees in biological sciences from Wichita State University.

We believe Dr. Weber is qualified to serve on our board of directors because of his broad range of experience in business and healthcare product development, including over a decade as the chief executive officer of companies developing locally delivered therapeutics.

Paul E. Cayer has served as our Chief Business Officer since October 2008, Chief Financial Officer since October 2010, and Secretary since February 2011. Mr. Cayer brings more than 25 years of experience in the pharmaceutical, medical device and healthcare technology field. Prior to joining our company, Mr. Cayer served from 2005 to 2008 as

Senior Vice President, Corporate Development for Verus Pharmaceuticals, Inc., a specialty pharmaceutical company focused on the treatment of allergic and respiratory disorders in children. From 2001 to 2005, Mr. Cayer served as the Chief Financial Officer and Senior Vice President, Business Development of Targeted Molecules Corporation, a biopharmaceutical company. Mr. Cayer has also held various management positions with Gensia Pharmaceuticals, Inc., a biopharmaceutical company, Acuson, a provider of medical

ultrasound systems, Castle & Cooke, a consumer products company, and served as consultant with Booz-Allen & Hamilton, a management and technology consulting firm. Mr. Cayer received his MBA and Bachelor s degree in biomechanical engineering from Harvard University.

Carl LeBel, Ph.D. has served as our Chief Scientific Officer since April 2009. Dr. LeBel has more than 25 years of pharmaceutical research and development experience. From 2003 to 2007, Dr. LeBel served as Executive Director and in a variety of other positions from 1993 to 2003 at Amgen, Inc., biopharmaceutical company. From 1991 to 1993, Dr. LeBel served as Research Scientist at Alkermes, Inc., a biopharmaceutical company. From 1990 to 1991, Dr. LeBel served as Consultant at Arthur D. Little, Inc., a management and technology consulting firm. He is also a scientific fellow of the American Academy of Otolaryngology Head & Neck Surgery, a full member of the Association for Research in Otolaryngology, and a full member of both the American Association for the Advancement of Science and the Society of Toxicology. Dr. LeBel received his Bachelor s degree in chemistry from the University of Detroit and a Ph.D. in Biomedical Sciences/Toxicology from Northeastern University.

Robert Michael Savel, II has served as our Chief Technical Officer since January 2014. From September 2011 to December 2013, Mr. Savel served as General Manager and Senior Vice President of Operations for Optimer Pharmaceuticals, Inc., a biopharmaceuticals company. From September 2010 to June 2011, Mr. Savel served as Senior Vice President and Chief Technical Officer for Inspire Pharmaceuticals, Inc., an ophthalmic pharmaceutical company. From April 2008 to September 2010, Mr. Savel served as President of Savel Enterprises LLC, a management consulting firm. From April 2007 to April 2008, Mr. Savel served as the Senior Vice President of Technical Operations for PDL BioPharma, an antibody manufacturer. Earlier in his career, he held leadership operating positions with Johnson & Johnson, a medical devices, pharmaceutical and consumer packaged goods manufacturer, which included the position of Vice President, Quality and Compliance. Mr. Savel received his Bachelor s degree in mechanical engineering from Virginia Polytechnic Institute and State University in Blacksburg, Virginia.

Anthony J. Yost has served as our Chief Commercial Officer since October 2014. From January 2012 to May 2014, Mr. Yost served as Chief Commercial Officer for Prometheus, Inc., a specialty pharmaceutical and diagnostic company. From August 2011 to January 2012, Mr. Yost served as Chief Commercial Officer for EKR Therapeutics, Inc., a specialty pharmaceutical company. From October 2010 to April 2011, he was the head of Sales and Marketing at PacificCord, a stem cell storage biotechnology company. From October 2008 to June 2010, Mr. Yost served as General Manager for the Western U.S. Operating Unit of Novartis AG, a pharmaceutical company. From November 2003 to September 2008, Mr. Yost served as President for Innovex North America, a pharmaceutical sales and marketing services division of Quintiles Transnational Corporation. From February 1998 to November 2003, he held various positions at Schering-Plough Corporation, a pharmaceutical manufacturing company, which included Vice President in the Acute Coronary Syndromes Business Unit, General Manager of Commercial and Manufacturing Operations in Portugal, Vice President of Managed Care and Vice President of the Cardiovascular Business Unit. Earlier in his career he worked for Boehringer Mannheim and Eli Lilly and Company. He is also currently a member of the board of directors of InSite Vision, Inc., a public company. Mr. Yost received his Bachelor s degree in pharmacy from Purdue University.

Non-Employee Directors

Peter Bisgaard has served as chairman of our board of directors since December 2013, and as a director since August 2010. Mr. Bisgaard is currently employed as a Partner at Novo Ventures (US) Inc., which provides consultancy services to Novo A/S, a Danish limited liability company that manages investments and financial assets. He joined Novo Ventures (US) Inc. in 2009. From 2001 to 2009, Mr. Bisgaard was employed as a Partner of Novo A/S. From 1998 to 2001, Mr. Bisgaard was employed with McKinsey & Co., a management consulting firm, where he focused on strategy development, mergers, acquisitions and alliances in various industries. He is also currently a member of

the board of directors of a number of private companies and is on the board of Alder

Biopharmaceuticals a publicly traded clinical-stage biopharmaceuticals company, and Nevro Corp., a publicly traded medical device company. Mr. Bisgaard holds an MSc from the Technical University of Denmark and was awarded a post graduate degree in mathematical modeling in economics by the European Consortium for Mathematics in the Industry.

We believe Mr. Bisgaard is qualified to serve on our board of directors and as our chairman because of his strong financial expertise, extensive industry experience, his experience of serving on the board of directors for several biopharmaceutical companies, and his experience with venture capital investments.

Vickie Capps has served on our board of directors since March 2014. From July 2002 to December 2013, Ms. Capps was the Chief Financial Officer of DJO Global, Inc. Ms. Capps joined DJO Global, Inc. in 2002. Prior to joining DJO Global, Inc., Ms. Capps served as the Chief Financial Officer of several other public and private companies. Earlier in her career, Ms. Capps was a Senior Audit and Accounting Professional at Ernst & Young LLP. Ms. Capps is currently a member of the Senior Advisory Board of Consonance Capital Partners, or CCP, a healthcare investment firm, and is an Executive Officer and a member of the board of directors of CCP s portfolio company, Eagle Rx, Inc. Ms. Capps is also a member of the board of directors of Connecture, Inc., a public company, and RF Surgical Systems, Inc., and is the chair of the audit committees of both companies. From 2007 to July 2010, Ms. Capps served as a member of the board of directors of SenoRx, Inc., prior to its acquisition by C. R. Bard, Inc. in July 2010. In addition, Ms. Capps serves as a member of the board of directors of the San Diego State University Research Foundation and is a member of its audit committee and its finance and investment committee. Ms. Capps is a California Certified Public Accountant and was recognized as CFO of the Year by the San Diego Business Journal in 2009 and 2010. Ms. Capps holds a Bachelor s degree in Business Administration/Accounting from San Diego State University.

We believe Ms. Capps is qualified to serve on our board of directors because of her exceptionally strong skill set consisting of corporate finance, accounting, operations, investor relations, capital markets and strategic business development.

Brian Dovey has served on our board of directors since August 2010. Mr. Dovey has been a Partner of Domain Associates, L.L.C., a private venture capital management firm focused on life sciences, since 1988. Prior to joining Domain, Mr. Dovey spent six years at Rorer Group, Inc. (now part of Sanofi-Aventis), including as President from 1986 to 1988. Previously, Mr. Dovey was president of Survival Technology, Inc., a start-up medical products company. He also held management positions with Howmedica, Inc., Howmet Corporation and New York Telephone Company. Mr. Dovey has served as both President and Chairman of the National Venture Capital Association. He is the former Chair, but now serves on the Board of Trustees, of the Wistar Institute, a leader in preclinical bio-medical research in the non-profit sector. Mr. Dovey serves on the board of directors and is also Chairman at the Center for Venture Education (Kauffman Fellows Program) and on the La Jolla Playhouse Board of Trustees. Mr. Dovey is also on the Venture Advisory Board of the Skolkovo Foundation. Mr. Dovey currently serves on the board of directors of public companies Orexigen Therapeutics, Inc., a biopharmaceutical company focused on the treatment of obesity, and REVA Medical, Inc., a medical device company. He is a trustee emeritus of Germantown Academy and is a former trustee of the University Of Pennsylvania School Of Nursing and the Burnham Institute for Medical Research. Mr. Dovey has also served as both president and chairman of the National Venture Capital Association. He was also a former board member of the industry associations representing the medical device industry as well as the association representing consumer pharmaceuticals. Mr. Dovey has also served as a member of the board of directors of the following publicly traded companies: Align Technology, Inc., Cardiac Science, Inc. and Neose Technologies, Inc. Mr. Dovey received his Bachelor s degree from Colgate University and an MBA from the Harvard Business School.

We believe Mr. Dovey is qualified to serve on our board of directors because of his experience serving as a director on over 35 private and public companies board of directors over the years, his experience with life science companies,

and his extensive experience at a healthcare venture capital firm.

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Chau Q. Khuong has served on our board of directors since August 2013. Mr. Khuong is currently employed as a Private Equity Partner at OrbiMed Advisers LLC, a venture capital and asset management firm, which he joined in 2003. He currently serves on the board of directors of Cerapedics, Inc., Aerpio Therapeutics, Inc., Inspire Medical Systems, Inc. and Pieris AG. Mr. Khuong received a Bachelor s degree in molecular biology with concentration in biotechnology and a Master s degree in Public Health with concentration in infectious diseases from Yale University.

We believe Mr. Khuong is qualified to serve on our board of directors because of his leadership experience, his extensive industry experience and his experience as a venture capital investor.

Jay Lichter, Ph.D. has served on our board of directors since May 2008. Dr. Lichter served as our Chief Executive Officer from inception until November 2010. He is an experienced biotechnology and pharmaceutical business executive with 25 years of experience in management, scientific research and business development. Since 2007, Dr. Lichter has been a managing director at Avalon Ventures, an early-stage venture capital fund focused on information technology and life sciences. In that role, he led Avalon s investments in and served as a director and chief executive officer for privately-held biotechnology companies Afraxis, Inc., Carolus Therapeutics, Inc., ReVision Therapeutics, Inc. and Zacharon Pharmaceuticals, Inc. He also currently serves on the board of directors of Aratana Therapeutics, Inc., a public company. Dr. Lichter also led Avalon s investments in or serves on the board of privately-held companies Sova Pharmaceuticals, Inc., Avelas Biosciences, Inc., COI Pharmaceuticals Inc. and Sitari Pharmaceuticals Corp. Dr. Lichter received a Bachelor s degree and Ph.D. in biochemistry from the University of Illinois. He also completed post-doctoral fellowships at Yale University and Du Pont Merck Pharmaceutical Company.

We believe Dr. Lichter is qualified to serve on our board of directors because of his experience as a venture capital investor and his experience as a biotechnology and pharmaceutical business executive with over 25 years of experience in management, scientific research and development.

John P. McKearn, Ph.D. has served on our board of directors since August 2010. Dr. McKearn joined RiverVest Venture Partners, a venture capital firm, in April 2008 as a Venture Partner and has been a Managing Director since April 2011. He currently serves on the board of directors of Allakos, Inc., a biopharmaceutical company. Prior to joining RiverVest, Dr. McKearn was the President and Chief Executive Officer of Kalypsys Inc., a biopharmaceutical company. From 2000 to June 2009, Dr. McKearn served on the board of IDM Pharma, Inc. (acquired by Takeda), a biotechnology company. He also previously served on the board of directors of Epimmune Inc., Keel Pharmaceuticals, Inc., ZS Pharma, Inc. and Lumena Pharmaceuticals, Inc. From 1987 to 2003, Dr. McKearn worked as a scientist with G.D. Searle & Company, which merged into Pharmacia Corporation in 2000, serving as the head of discovery research from 1997 to 2003. Before that, he was a senior scientist at E.I. DuPont de Nemours and Company; a member of the Basel Institute for Immunology in Basel, Switzerland; and a research associate in the Department of Microbiology and Immunology at Washington University in St. Louis. Dr. McKearn holds a Bachelor s degree in biology from Northern Illinois University and a Ph.D. in immunology from the University of Chicago.

We believe Dr. McKearn is qualified to serve on our board of directors because of his experience as a venture capital investor, his industry expertise, and his leadership experience with biotechnology and pharmaceutical companies.

Heather Preston, M.D. has served on our board of directors since August 2010. Dr. Preston is currently employed as a Partner and Managing Director of TPG Biotech, a biotechnology venture capital firm. Dr. Preston joined TPG in 2005. She currently serves on the board of directors of Alder Biopharmaceuticals, Inc., a public company and on the boards of a number of private companies. Prior to joining TPG Biotech, Dr. Preston served for two years as a medical device and biotechnology venture capital investor at JP Morgan Partners, LLC, a private equity firm. Prior to that, she was an Entrepreneur-in-Residence at New Enterprise Associates, a venture capital firm. From 1997 to 2002,

Dr. Preston served as a leader of the pharmaceutical and medical products

consulting practice at McKinsey & Co. in New York. Dr. Preston holds a Bachelor s degree in biochemistry from the University of London and an MD from the University of Oxford. After leaving Oxford, Dr. Preston completed a post-doctoral fellowship in molecular biology at the Dana Farber Cancer Institute, Harvard University. Dr. Preston completed her training in Internal Medicine at the Massachusetts General Hospital and then sub-specialized in Gastroenterology and Hepatology at U.C.S.F. During Dr. Preston s academic career, she was the recipient of a Fulbright Scholarship, a Fulbright Cancer Research Scholarship, a Harlech Scholarship and a Science and Engineering Research Council Post-doctoral Fellowship Award.

We believe Dr. Preston is qualified to serve on our board of directors because of her experience as an investor in biopharmaceutical and life sciences companies, her educational background, and leadership in the medical and life science industries.

Board Composition

Our business and affairs are managed under the direction of our board of directors. The number of directors is fixed by our board of directors, subject to the terms of our amended and restated certificate of incorporation and amended and restated bylaws. Our board of directors currently consists of eight directors, six of whom qualify as independent under NASDAQ listing standards.

In accordance with our amended and restated certificate of incorporation and our amended and restated bylaws, our board of directors is divided into three classes with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. Our directors are divided among the three classes as follows:

- the Class I directors are Brian Dovey and John McKearn, Ph.D., and their terms will expire at the annual meeting of stockholders to be held in 2015;
- the Class II directors are Peter Bisgaard, Chau Q. Khuong and Jay Lichter, Ph.D., and their terms will expire at the annual meeting of stockholders to be held in 2016; and
- the Class III directors are Vickie Capps, Heather Preston, M.D. and David A. Weber, Ph.D., and their terms will expire at the annual meeting of stockholders to be held in 2017.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our management or a change of control. Under Delaware law, our directors may be removed for cause by the affirmative vote of the holders of a majority of our outstanding voting stock. Directors may not be removed by our stockholders without cause.

Any increase or decrease in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors.

Director Independence

Our common stock is listed on The NASDAQ Global Select Market. Under the rules of NASDAQ, independent directors must comprise a majority of a listed company s board of directors within one year of the company s listing

date. In addition, the rules of NASDAQ require that, subject to specified exceptions, each member of a listed company s audit, compensation and nominating and governance committees be independent. Audit committee members and compensation members must also satisfy separate independence criteria set forth in Rule 10A-3 and Rule 10C-1, respectively, under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Under the rules of NASDAQ, a director will only qualify as an independent director if, among other things, in the opinion of that company s board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

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To be considered independent for purposes of Rule 10A-3 and under the rules of NASDAQ, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, board of directors, or any other board committee: (1) accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries; or (2) be an affiliated person of the listed company or any of its subsidiaries.

To be considered independent for purposes of Rule 10C-1 and under the rules of NASDAQ, the board of directors must affirmatively determine that the member of the compensation committee is independent, including a consideration of all factors specifically relevant to determining whether the director has a relationship to the company which is material to that director s ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: (i) the source of compensation of such director, including any consulting, advisory or other compensatory fee paid by the company to such director; and (ii) whether such director is affiliated with the company, a subsidiary of the company or an affiliate of a subsidiary of the company.

Our board of directors undertook a review of its composition, the composition of its committees and the independence of our directors and considered whether any director has a material relationship with us that could compromise his or her ability to exercise independent judgment in carrying out his or her responsibilities. Based upon information requested from and provided by each director concerning his background, employment and affiliations, including family relationships, our board of directors has determined that none of Messrs. Bisgaard, Dovey and Khuong, Drs. Lichter, McKearn and Preston, and Ms. Capps, representing seven of our eight directors, has a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is independent as that term is defined under the rules of NASDAQ.

In making these determinations, our board of directors considered the current and prior relationships that each non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director, and the transactions involving them described in the section titled Certain Relationships and Related Party Transactions. In evaluating Dr. Lichter s independence, our board of directors considered Dr. Lichter s position as managing director at Avalon Ventures, and the various arrangements pursuant to which Avalon-affiliated entities and we shared common services, as described in the section titled Certain Relationships and Related Party Transactions Arrangements with Avalon-Affiliated Entities. Pursuant to such arrangements, we made payments to Avalon-affiliated entities in excess of $200,000 in fiscal year 2011, but payments did not exceed $200,000 in fiscal years 2012, 2013 or 2014. Therefore, our board of directors concluded that Dr. Lichter was not independent as that term is defined under the rules of NASDAQ until January 1, 2015. As of January 1, 2015, Dr. Lichter met the requirements for independence under the rules of NASDAQ.

There are no family relationships among any of our directors or executive officers.

Board Leadership Structure

Our board of directors is currently chaired by Mr. Bisgaard. As a general policy, our board of directors believes that separation of the positions of Chairman and Chief Executive Officer reinforces the independence of the board of directors from management, creates an environment that encourages objective oversight of management s performance and enhances the effectiveness of the board of directors as a whole. As such, Dr. Weber serves as our President and Chief Executive Officer while Mr. Bisgaard serves as our Chairman of the board of directors but is not an officer. We expect and intend the positions of Chairman of the board of directors and Chief Executive Officer to continue to be held by two individuals in the future.

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Role of the Board in Risk Oversight

One of the key functions of our board of directors is informed oversight of our risk management process. Our board of directors does not have a standing risk management committee, but rather administers this oversight function directly through the board of directors as a whole, as well as through its standing committees that address risks inherent in their respective areas of oversight. In particular, our board of directors is responsible for monitoring and assessing strategic risk exposure. Our audit committee is responsible for reviewing and discussing our major financial risk exposures and the steps our management has taken to monitor and control these exposures, including guidelines and policies with respect to risk assessment and risk management. Our audit committee also monitors compliance with legal and regulatory requirements and reviews related party transactions, in addition to oversight of the performance of our external audit function. Our corporate governance and nominating committee monitors the effectiveness of our corporate governance guidelines. Our compensation committee assesses and monitors whether any of our compensation policies and programs has the potential to encourage excessive risk-taking.

Board Committees

Our board of directors has an audit committee, a compensation committee, and a corporate governance and nominating committee, each of which has the composition and the responsibilities described below.

Audit Committee

Our audit committee is comprised of Ms. Capps, Mr. Khoung, and Drs. Lichter and McKearn. Ms. Capps serves as the chairperson of our audit committee. All members of our audit committee meet the requirements for independence and financial literacy of audit committee members under current NASDAQ listing standards and SEC rules and regulations. Our board of directors has determined that Ms. Capps is an audit committee financial expert as defined under the applicable rules of the SEC and has the requisite financial sophistication as defined under NASDAQ listing standards. The responsibilities of our audit committee include, among other things:

selecting and hiring the independent registered public accounting firm to audit our financial statements;

helping to ensure the independence and performance of the independent registered public accounting firm;

approving audit and non-audit services and fees;

reviewing financial statements and discussing with management and the independent registered public accounting firm our annual audited and quarterly financial statements, the results of the independent audit and the quarterly reviews, and the reports and certifications regarding internal controls over financial reporting and disclosure controls;

preparing the audit committee report that the SEC requires to be included in our annual proxy statement;

- reviewing reports and communications from the independent registered public accounting firm;
- reviewing the adequacy and effectiveness of our internal controls and disclosure controls and procedures;
- reviewing our policies on risk assessment and risk management;
- reviewing related party transactions; and
- establishing and overseeing procedures for the receipt, retention and treatment of accounting related complaints and the confidential submission by our employees of concerns regarding questionable accounting or auditing matters.

Our audit committee operates under a written charter, which satisfies the applicable rules of the SEC and the listing standards of NASDAQ.

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Compensation Committee

Our compensation committee is comprised of Messrs. Bisgaard and Khuong and Dr. Lichter. Dr. Lichter serves as the chairperson of our compensation committee. All members of our compensation committee meet the requirements for independence under current NASDAQ listing standards and SEC rules and regulations. Each member of the compensation committee is also a non-employee director, as defined pursuant to Rule 16b-3 promulgated under the Exchange Act, and Messrs. Bisgaard and Khuong are each an outside director, as defined pursuant to Section 162(m) of the Internal Revenue Code, as amended. The purpose of our compensation committee is to oversee our compensation policies, plans and benefit programs and to discharge the responsibilities of our board of directors relating to compensation of our executive officers. The responsibilities of our compensation committee include, among other things:

- overseeing our overall compensation philosophy and compensation policies, plans and benefit programs;
- reviewing and approving or recommending to the board for approval compensation for our executive officers and directors;
- preparing the compensation committee report that the SEC will require to be included in our annual proxy statement; and
- administering our equity compensation plans.

Our compensation committee operates under a written charter, which satisfies the applicable rules of the SEC and the listing standards of NASDAQ.

Corporate Governance and Nominating Committee

Our corporate governance and nominating committee is comprised of Messrs. Dovey and Khuong and Dr. Preston. Dr. Preston serves as the chairperson of our corporate governance and nominating committee. All members of our corporate governance and nominating committee meet the requirements for independence under current NASDAQ listing standards and SEC rules and regulations. The responsibilities of our corporate governance and nominating committee include, among other things:

- identifying, evaluating and making recommendations to our board of directors regarding nominees for election to our board of directors and its committees;
- considering and making recommendations to our board of directors regarding the composition of our board of directors and its committees;
- reviewing developments in corporate governance practices;

evaluating the adequacy of our corporate governance practices and reporting; and

evaluating the performance of our board of directors and of individual directors.

Our corporate governance and nominating committee operates under a written charter, which satisfies the applicable rules of the SEC and the listing standards of NASDAQ. We intend to comply with future requirements to the extent they become applicable to us.

Compensation Committee Interlocks and Insider Participation

None of our executive officers serves, or in the past has served, as a member of the board of directors or compensation committee, or other committee serving an equivalent function, of any entity that has one or more executive officers who serve as members of our board of directors or our compensation committee. None of the members of our compensation committee is, or has ever been, an officer or employee of our company, except for Dr. Lichter who previously served as our Chief Executive Officer from May 2008 until November 2010.

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Code of Business Conduct and Ethics

Our board of directors has adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions and agents and representatives, including consultants. A copy of the code of business conduct and ethics is available on our website at www.otonomy.com. We intend to disclose future amendments to such code, or any waivers of its requirements, applicable to any principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions or our directors on our website identified above. The inclusion of our website address in this prospectus does not include or incorporate by reference the information on our website into this prospectus.

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EXECUTIVE COMPENSATION

Our named executive officers for 2014, which consist of our principal executive officer and the next two most highly compensated executive officers, are:

David A. Weber, Ph.D., President and Chief Executive Officer;

Paul E. Cayer, Chief Financial and Business Officer, and Secretary; and

Anthony J. Yost, Chief Commercial Officer.

Summary Compensation Table

The following table provides information regarding the compensation of our named executive officers during the years ended December 31, 2013 and 2014.

Name and Principal Position	Year	Salary ($)	Bonus ($)[1]	Option Awards ($)[2]	Total ($)
David A. Weber, Ph.D.	2013	$ 428,500	$ 107,125	$ 559,052	$ 1,094,677
President and Chief Executive Officer	2014	455,188	237,500	4,097,840	4,790,528
Paul E. Cayer	2013	305,000	61,000	180,467	546,467
Chief Financial and Business Officer, and Secretary	2014	331,711	140,000	1,771,134	2,242,845
Anthony J. Yost [3]	2013				
Chief Commercial Officer	2014	68,472		2,826,684	2,895,156

(1) This column reflects bonus payments earned in 2013 and 2014.

(2) This column reflects the aggregate grant date fair value of stock options granted during 2013 and 2014 computed in accordance with the provisions of Accounting Standards Codification (ASC) 718, Compensation Stock Compensation. The assumptions that we used to calculate these amounts are discussed in Note 8 to our financial statements appearing at the end of this prospectus. These amounts do not reflect the actual economic value that will be realized by the named executive officer upon the vesting of the stock options, the exercise of the stock options, or the sale of the common stock underlying such stock options.

(3) Mr. Yost joined our company on October 20, 2014.

Outstanding Equity Awards at Fiscal Year-End 2014

The following table provides information regarding equity awards held by our named executive officers as of December 31, 2014.

	Option Awards				
		Number of Securities Underlying Unexercised Options			
Name	Vesting Commencement Date	Exercisable	Unexercisable	Option Exercise Price	Option Expiration Date
David A. Weber, Ph.D.	11/21/10	95,420[1]		$ 3.17	11/21/20
	5/18/11	57,414[2]		$ 3.17	6/15/21
	9/1/13	250,951[3]	170,454	$ 1.76	12/20/23
	4/23/2014	242,747[4]		$ 6.33	6/3/24
	12/11/14		130,000[5]	$ 34.12	12/11/24

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		Option Awards			
		Number of Securities Underlying Unexercised Options			
Name	Vesting Commencement Date	Exercisable	Unexercisable	Option Exercise Price	Option Expiration Date
Paul E. Cayer	6/16/10	8,532[6]		$ 2.82	6/16/20
	11/19/10	29,863[7]		$ 3.17	11/19/20
	9/18/12	11,198[8]	8,710	$ 1.06	9/18/22
	9/1/13	44,231[9]	97,310	$ 1.76	12/20/23
	4/23/2014	[10]	85,039	$ 6.33	6/3/24
	12/11/14	[11]	60,000	$ 34.12	12/11/24
Anthony J. Yost	10/20/14	[12]	180,000	$ 22.74	10/20/24

(1) The option vested with respect to 25% of the shares subject to the option on November 21, 2011, and 1/36th of the remaining shares subject to the option vested monthly thereafter subject to continued service through each vesting date. All of the shares underlying this option are subject to an early exercise provision.

(2) The option vested with respect to 25% of the shares subject to the option on May 18, 2012, and 1/36th of the remaining shares subject to the option vest monthly thereafter subject to continued service through each vesting date. All of the shares underlying this option are subject to an early exercise provision.

(3) The option vests with respect to 25% of the shares subject to the option on September 1, 2014, and 1/36th of the remaining shares subject to the option vest monthly thereafter subject to continued service through each vesting date. 210,938 shares underlying this option are subject to an early exercise provision, of which 17,064 shares were early exercised on February 15, 2014.

(4) The option vests with respect to 25% of the shares subject to the option on April 23, 2015, and 1/36th of the remaining shares subject to the option vest monthly thereafter subject to continued service through each vesting date. All of the shares underlying this option are subject to an early exercise provision.

(5) The option vests with respect to 25% of the shares subject to the option on December 11, 2015, and 1/36th of the remaining shares subject to the option vest monthly thereafter subject to continued service through each vesting date.

(6) The option vested with respect to 25% of the shares subject to the option on June 16, 2011, and 1/36th of the remaining shares subject to the option vested monthly thereafter subject to continued service through each vesting date.

(7) The option vested with respect to 25% of the shares subject to the option on November 19, 2011, and 1/36th of the remaining shares subject to the option vested monthly thereafter subject to continued service through each vesting date.

(8) The option vested with respect to 25% of the shares subject to the option on September 18, 2013, and 1/36th of the remaining shares subject to the option vest monthly thereafter subject to continued service through each vesting date.

(9) The option vests with respect to 25% of the shares subject to the option on September 1, 2014, and 1/36th of the remaining shares subject to the option vest monthly thereafter subject to continued service through each vesting date.

(10) The option vests with respect to 25% of the shares subject to the option on April 23, 2015, and 1/36th of the remaining shares subject to the option vest monthly thereafter subject to continued service through each vesting date.

(11) The option vests with respect to 25% of the shares subject to the option on December 11, 2015, and 1/36th of the remaining shares subject to the option vest monthly thereafter subject to continued service through each vesting date.

(12) The option vests with respect to 25% of the shares subject to the option on October 20, 2015, and 1/36th of the remaining shares subject to the option vest monthly thereafter subject to continued service through each vesting date.

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Executive Employment Agreements

David A. Weber, Ph.D.

We entered into an employment agreement with Dr. Weber effective as of the effective date of our initial public offering. The employment agreement has an initial term of 4 years, subject to earlier termination as provided in the employment agreement. Unless either party gives at least 90 days notice prior to the expiration of the initial term or the then-current additional term, as applicable, the employment agreement shall be renewed for an additional term of 1 year, in each case, commencing on the expiration of the initial term or the then-current additional term, as the case may be, subject to earlier termination as provided in the employment agreement. In the event of a change of control (as defined in the employment agreement), if there is less than 12 months remaining in the initial term or then-current additional term, as applicable, the term will automatically extend until the 12 month anniversary following the change of control. Pursuant to the agreement, Dr. Weber will continue to serve as our President and Chief Executive Officer on an at will basis. Dr. Weber s employment agreement provides for a base salary of $475,000, which was subsequently increased to $500,000 effective as of January 1, 2015, eligibility to receive an annual performance bonus with the target amount determined as 50% of Dr. Weber s annual base salary, and eligibility to participate in employee benefit or group insurance plans maintained from time to time by us. Dr. Weber s employment agreement also provides that he will continue to serve as a member of our board of directors during the term of his employment subject to board and/or stockholder approval.

Pursuant to the employment agreement of Dr. Weber, if we terminate the employment of Dr. Weber other than for death, disability, or cause or Dr. Weber resigns for good reason (as such terms are defined in Dr. Weber s employment agreement), and, within 60 days following his termination, Dr. Weber executes a waiver and release of claims in our favor and resigns from all positions he may hold as an officer or director, Dr. Weber is entitled to receive (i) continuing payments of his then-current base salary for a period of 12 months, payable pursuant to our regular payroll procedures, (ii) an amount equal to a pro rata portion of his target annual bonus for the year of termination, payable in accordance with our regular payroll procedures, (iii) reimbursement of premiums to maintain group health insurance continuation benefits pursuant to COBRA for him and his respective dependents for up to 12 months, and (iv) additional vesting and exercisability as to any outstanding equity awards held by him as if he had remained our employee for an additional 24 months.

Pursuant to the employment agreement of Dr. Weber, if, within the 3 month period prior to or the 12 month period following a change of control (as defined in Dr. Weber s employment agreement), the employment of Dr. Weber is terminated under the circumstances described in the above paragraph and, within 60 days following his termination, Dr. Weber executes a waiver and release of claims in our favor and resigns from all positions he may hold as an officer or director, Dr. Weber is entitled to receive (i) a lump sum payment equal to 18 months of his then-current base salary, payable pursuant to our regular payroll procedures, (ii) a lump sum payment equal to 150% of the higher of (x) his full target annual bonus for the fiscal year of termination, or (y) his full target annual bonus for the fiscal year in which the change of control occurs, payable pursuant to our regular payroll procedures, (iii) reimbursement of premiums to maintain group health insurance continuation benefits pursuant to COBRA for him and his respective dependents for up to 18 months, and (iv) vesting acceleration of 100% with respect to any outstanding equity awards held by him on the date of his termination.

In the event any payment to Dr. Weber pursuant to his employment agreement would be subject to the excise tax imposed by Section 4999 of the Internal Revenue Code, as amended, or the Code (as a result of a payment being classified as a parachute payment under Section 280G of the Code), Dr. Weber will receive such payment as would entitle him to receive the greatest after-tax benefit, even if it means that we pay him a lower aggregate payment so as to minimize or eliminate the potential excise tax imposed by Section 4999 of the Code.

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Paul E. Cayer

We entered into an employment agreement with Mr. Cayer effective as of the effective date of our initial public offering. The employment agreement has an initial term of 4 years, subject to earlier termination as provided in the employment agreement. Unless either party gives at least 90 days notice prior to the expiration of the initial term or the then-current additional term, as applicable, the employment agreement shall be renewed for an additional term of 1 year, in each case, commencing on the expiration of the initial term or the then-current additional term, as the case may be, subject to earlier termination as provided in the employment agreement. In the event of a change of control (as defined in the employment agreement), if there is less than 12 months remaining in the initial term or then-current additional term, as applicable, the term will automatically extend until the 12 month anniversary following the change of control. Pursuant to the agreement, Mr. Cayer will continue to serve as our Chief Financial and Business Officer on an at will basis. Mr. Cayer s employment agreement provides for a base salary of $350,000, which was subsequently increased to $360,500 effective as of January 1, 2015, eligibility to receive an annual performance bonus with the target amount determined as 40% of Mr. Cayer s annual base salary, and eligibility to participate in employee benefit or group insurance plans maintained from time to time by us.

Pursuant to the employment agreement of Mr. Cayer, if we terminate the employment of Mr. Cayer other than for death, disability, or cause or Mr. Cayer resigns for good reason (as such terms are defined in Mr. Cayer s employment agreement), and, within 60 days following his termination, Mr. Cayer executes a waiver and release of claims in our favor and resigns from all positions he may hold as an officer or director, Mr. Cayer is entitled to receive (i) continuing payments of his then-current base salary for a period of 9 months, payable pursuant to our regular payroll procedures, (ii) an amount equal to a pro rata portion of his target annual bonus for the year of termination, payable in accordance with our regular payroll procedures, (iii) reimbursement of premiums to maintain group health insurance continuation benefits pursuant to COBRA for him and his respective dependents for up to 9 months, and (iv) additional vesting and exercisability as to any outstanding equity awards held by him as if he had remained our employee for an additional 12 months.

Pursuant to the employment agreement of Mr. Cayer, if, within the 3 month period prior to or the 12 month period following a change of control (as defined in Mr. Cayer s employment agreement), the employment of Mr. Cayer is terminated under the circumstances described in the above paragraph and, within 60 days following his termination, Mr. Cayer executes a waiver and release of claims in our favor and resigns from all positions he may hold as an officer or director, Mr. Cayer is entitled to receive (i) a lump sum payment equal to 12 months of his then-current base salary, payable pursuant to our regular payroll procedures, (ii) a lump sum payment equal to the higher of (x) his full target annual bonus for the fiscal year of termination, or (y) his full target annual bonus for the fiscal year in which the change of control occurs, payable pursuant to our regular payroll procedures, (iii) reimbursement of premiums to maintain group health insurance continuation benefits pursuant to COBRA for him and his respective dependents for up to 12 months, and (iv) vesting acceleration of 100% with respect to any outstanding equity awards held by him on the date of his termination.

In the event any payment to Mr. Cayer pursuant to his employment agreement would be subject to the excise tax imposed by Section 4999 of the Code (as a result of a payment being classified as a parachute payment under Section 280G of the Code), Mr. Cayer will receive such payment as would entitle him to receive the greatest after-tax benefit, even if it means that we pay him a lower aggregate payment so as to minimize or eliminate the potential excise tax imposed by Section 4999 of the Code.

Anthony J. Yost

We entered into an employment agreement with Mr. Yost, dated October 20, 2014. The employment agreement has an initial term of 4 years, subject to earlier termination as provided in the employment agreement. Unless either party gives at least 90 days notice prior to the expiration of the initial term or the then-current additional term, as applicable, the employment agreement shall be renewed for an additional term of 1 year, in

each case, commencing on the expiration of the initial term or the then-current additional term, as the case may be, subject to earlier termination as provided in the employment agreement. In the event of a change of control (as defined in the employment agreement), if there is less than 12 months remaining in the initial term or then-current additional term, as applicable, the term will automatically extend until the 12 month anniversary following the change of control. Pursuant to the agreement, Mr. Yost will serve as our Chief Commercial Officer on an at will basis. Mr. Yost s employment agreement provides for a base salary of $340,000, eligibility to receive an annual performance bonus beginning in 2015 with the target amount determined as 40% of Mr. Yost s annual base salary, and eligibility to participate in employee benefit or group insurance plans maintained from time to time by us.

Pursuant to the employment agreement of Mr. Yost, if we terminate the employment of Mr. Yost other than for death, disability, or cause or Mr. Yost resigns for good reason (as such terms are defined in Mr. Yost s employment agreement), and, within 60 days following his termination, Mr. Yost executes a waiver and release of claims in our favor and resigns from all positions he may hold as an officer or director, Mr. Yost is entitled to receive (i) continuing payments of his then-current base salary for a period of 9 months, payable pursuant to our regular payroll procedures, (ii) an amount equal to a pro rata portion of his target annual bonus for the year of termination, payable in accordance with our regular payroll procedures, (iii) reimbursement of premiums to maintain group health insurance continuation benefits pursuant to COBRA for him and his respective dependents for up to 9 months, and (iv) additional vesting and exercisability as to any outstanding equity awards held by him as if he had remained our employee for an additional 12 months. Notwithstanding the foregoing, if, prior to April 20, 2015, the employment of Mr. Yost is terminated under the circumstances described in this paragraph, Mr. Yost will only be eligible to receive continuing payments of his then-current base salary for a period of 3 months, payable pursuant to our regular payroll procedures, and no other severance benefits.

Pursuant to the employment agreement of Mr. Yost, if, within the 3 month period prior to or the 12 month period following a change of control (as defined in Mr. Yost s employment agreement), the employment of Mr. Yost is terminated under the circumstances described in the above paragraph and, within 60 days following his termination, Mr. Yost executes a waiver and release of claims in our favor and resigns from all positions he may hold as an officer or director, Mr. Yost is entitled to receive (i) a lump sum payment equal to 12 months of his then-current base salary, payable pursuant to our regular payroll procedures, (ii) a lump sum payment equal to the higher of (x) his full target annual bonus for the fiscal year of termination, or (y) his full target annual bonus for the fiscal year in which the change of control occurs, payable pursuant to our regular payroll procedures, (iii) reimbursement of premiums to maintain group health insurance continuation benefits pursuant to COBRA for him and his respective dependents for up to 12 months, and (iv) vesting acceleration of 100% with respect to any outstanding equity awards held by him on the date of his termination.

In the event any payment to Mr. Yost pursuant to his employment agreement would be subject to the excise tax imposed by Section 4999 of the Code (as a result of a payment being classified as a parachute payment under Section 280G of the Code), Mr. Yost will receive such payment as would entitle him to receive the greatest after-tax benefit, even if it means that we pay him a lower aggregate payment so as to minimize or eliminate the potential excise tax imposed by Section 4999 of the Code.

Director Compensation

Each non-employee director is eligible to receive compensation for his or her service consisting of annual cash retainers and equity awards. We also reimburse our directors for expenses associated with attending meetings of our board of directors and committees of our board of directors. All non-employee directors are entitled to receive the following cash compensation for their services:

$35,000 per year for service as a board member;

$20,000 per year additionally for service as chairman of the board;

$15,000 per year additionally for service as chairman of the audit committee;

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$7,500 per year additionally for service as an audit committee member;

$10,000 per year additionally for service as chairman of the compensation committee;

$5,000 per year additionally for service as a compensation committee member;

$7,500 per year additionally for service as chairman of the corporate governance and nominating committee; and

$3,750 per year additionally for service as a corporate governance and nominating committee member.

All cash payments to non-employee directors will be paid quarterly in arrears on a prorated basis.

In addition, each non-employee director automatically will be granted an initial award of a nonstatutory stock option to purchase 25,000 shares of our common stock effective on the date on which such person first becomes elected as a non-employee director. Such initial award will vest as to one-third of the shares subject thereto on each anniversary of the initial award s grant date, provided that the director remains a service provider through the applicable vesting date. On the date of each annual meeting of our stockholders beginning with the first annual meeting following our initial public offering, each non-employee director automatically will be granted a nonstatutory stock option to purchase 15,000 shares of our common stock. Such annual award will vest fully on the date of the next annual meeting held after the date of grant, provided that the director remains a service provider through the applicable vesting date.

Our 2014 Plan, as described below under the section titled Employee Benefit and Stock Plans, provides that in the event of a merger or change in control, as defined in our 2014 Plan, each outstanding equity award granted under our 2014 Plan that is held by a non-employee director will fully vest, all restrictions on the shares subject to such award will lapse, and with respect to awards with performance-based vesting, all performance goals or other vesting criteria will be deemed achieved at 100% of target levels, and all of the shares subject to such award will become fully exercisable, if applicable.

The following table sets forth information regarding compensation earned by or paid to our non-employee directors during 2014:

Name	Fees Earned or Paid in Cash ($)	Option Awards ($)[1]	Total ($)
Peter Bisgaard [2]			
Vickie Capps [3]	$ 41,667	$ 47,099	$ 88,766
Brian Dovey	15,000		15,000
Chau Q. Khuong	19,839		19,839
Jay Lichter, Ph.D.	20,323		20,323
John P. McKearn, Ph.D.[4]			
Heather Preston, M.D.	16,452		16,452
Jeffrey Harris, M.D., Ph.D [5]			

(1) This column reflects the aggregate grant date fair value of stock options granted during 2014 computed in accordance with the provisions of Accounting Standards Codification (ASC) 718, Compensation Stock Compensation. The assumptions that we used to calculate these amounts are discussed in Note 8 to our financial statements appearing at the end of this prospectus. These amounts do not reflect the actual economic value that will be realized by the director upon the vesting of the stock options, the exercise of the stock options, or the sale of the common stock underlying such stock options.
(2) Mr. Bisgaard declined compensation for 2014.
(3) Ms. Capps joined our board of directors in March 2014.
(4) Dr. McKearn declined compensation for 2014.
(5) Dr. Harris resigned from our board of directors on March 3, 2014.

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The following table lists all outstanding equity awards held by our non-employee directors as of December 31, 2014.

Name	Option Grant Date	Number of Securities Underlying Unexercised Options Exercisable	Number of Securities Underlying Unexercised Options Unexercisable	Option Exercise Price Per Share	Option Expiration Date
Peter Bisgaard					
Vickie Capps[1]					
Brian Dovey					
Chau Q. Khuong					
Jay Lichter, Ph.D.					
John P. McKearn, Ph.D.					
Heather Preston, M.D.					
Jeffrey Harris, M.D., Ph.D.[2]	6/16/10	5,688[3]		$ 2.82	6/16/20
	11/19/10	3,965[4]		$ 3.17	11/19/20
	6/15/11	4,845[5]	564	$ 3.17	6/15/21

(1) Ms. Capps joined our board of directors in March 2014. Ms. Capps was granted an option to purchase 14,220 shares of common stock on March 6, 2014 at an exercise price of $1.76 per share. 1/24 of the option vested on April 6, 2014, and 1/24 of the remaining shares subject to the option vest monthly thereafter subject to continued service through each vesting date. All of the shares underlying the option are subject to an early exercise provision, and all shares were early exercised on April 9, 2014. In addition, Ms. Capps was granted an option to purchase 7,110 shares of common stock on June 3, 2014 at an exercise price of $6.33 per share. 1/24 of the option vested on May 23, 2014, and 1/24 of the remaining shares subject to the option vest monthly thereafter subject to continued service through each vesting date. All of the shares underlying the option are subject to an early exercise provision, and all shares were early exercised on July 10, 2014.

(2) Dr. Harris resigned from our board of directors on March 3, 2014.

(3) The option vested with respect to 25% of the shares subject to the option on June 16, 2011, and 1/36th of the remaining shares subject to the option vested monthly thereafter subject to continued service through each vesting date.

(4) The option vested with respect to 25% of the shares subject to the option on November 19, 2011, and 1/36th of the remaining shares subject to the option vested monthly thereafter subject to continued service through each vesting date.

(5) The option vested with respect to 25% of the shares subject to the option on May 18, 2012, and 1/36th of the remaining shares subject to the option vest monthly thereafter subject to continued service through each vesting date.

Employee Benefit and Stock Plans

2014 Equity Incentive Plan

Our board of directors adopted the 2014 Equity Incentive Plan, or the 2014 Plan, in connection with our initial public offering. Our 2014 Plan permits the grant of incentive stock options, within the meaning of Section 422 of the Code,

to our employees and any parent and subsidiary corporations employees, and for the grant of nonstatutory stock options, restricted stock, restricted stock units, stock appreciation rights, performance units and performance shares to our employees, directors and consultants and our parent and subsidiary corporations employees and consultants.

Authorized shares. As of September 30, 2014, a total of 2,220,000 shares of our common stock were reserved for issuance pursuant to the 2014 Plan, of which options to purchase 4,200 shares of our common stock were outstanding, and 2,215,800 shares remained available for issuance. In addition, the shares reserved for

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issuance under our 2014 Plan include shares reserved but not issued under the 2010 Equity Incentive Plan, and shares subject to stock options or similar awards granted under the 2010 Equity Incentive Plan that expire or terminate without having been exercised in full and shares issued pursuant to awards granted under the 2010 Equity Incentive Plan that are forfeited to or repurchased by us (provided that the maximum number of shares that may be added to the 2014 Plan pursuant to this sentence is 2,480,500 shares). In addition, shares may become available under the 2014 Plan under the following two paragraphs.

The number of shares available for issuance under the 2014 Plan will also include an annual increase on the first day of each fiscal year beginning in 2015, equal to the least of:

2,500,000 shares;

5% of the outstanding shares of common stock as of the last day of our immediately preceding fiscal year; or

such other amount as our board of directors may determine.

Under this provision, an additional 1,058,663 shares were added to the 2014 Plan s share reserve effective January 1, 2015.

If an award expires or becomes unexercisable without having been exercised in full, is surrendered pursuant to an exchange program, or, with respect to restricted stock, restricted stock units, performance units or performance shares, is forfeited or repurchased due to failure to vest, the unpurchased shares (or for awards

other than stock options or stock appreciation rights, the forfeited or repurchased shares) will become available for future grant or sale under our 2014 Plan. With respect to stock appreciation rights, the net shares issued will cease to be available under the 2014 Plan and all remaining shares will remain available for future grant or sale under the 2014 Plan. Shares used to pay the exercise price of an award or satisfy the tax withholding obligations related to an award will become available for future grant or sale under our 2014 Plan. To the extent an award is paid out in cash rather than shares, such cash payment will not result in reducing the number of shares available for issuance under our 2014 Plan.

Plan administration. Our board of directors or one or more committees appointed by our board of directors administers our 2014 Plan. Our board of directors has appointed our compensation committee to administer the 2014 Plan. In the case of awards intended to qualify as performance-based compensation within the meaning of Section 162(m) of the Code, the committee will consist of two or more outside directors within the meaning of Section 162(m). In addition, if we determine it is desirable to qualify transactions under the 2014 Plan as exempt under Rule 16b-3 of the Exchange Act or Rule 16b-3, such transactions will be structured to satisfy the requirements for exemption under Rule 16b-3. Subject to the provisions of our 2014 Plan, the administrator has the power to administer the plan, including but not limited to, the power to interpret the terms of our 2014 Plan and awards granted under it, to create, amend and revoke rules relating to our 2014 Plan, including creating sub-plans, and to determine the terms of the awards, including the exercise price, the number of shares subject to each such award, the exercisability of the awards and the form of consideration, if any, payable upon exercise. The administrator also has the authority to amend existing awards to reduce or increase their exercise price, to allow participants the opportunity to transfer outstanding awards to a financial institution or other person or entity selected by the administrator and to institute an exchange program by which outstanding awards may be surrendered in exchange for awards of the same

type which may have a higher or lower exercise price or different terms, awards of a different type and/or cash.

Stock options. Stock options may be granted under our 2014 Plan. The exercise price of options granted under our 2014 Plan must at least be equal to the fair market value of our common stock on the date of grant. The term of an incentive stock option may not exceed 10 years, except that with respect to any participant who owns more than 10% of the voting power of all classes of our outstanding stock, the term must not exceed five years and the exercise price must equal at least 110% of the fair market value on the grant date. The administrator will determine the methods of payment of the exercise price of an option, which may include cash, shares or other

property acceptable to the administrator, as well as other types of consideration permitted by applicable law. After the termination of service of an employee, director or consultant, he or she may exercise his or her option for the period of time stated in his or her option agreement. Generally, if termination is due to death or disability, the option will remain exercisable for 12 months. In all other cases, the option will generally remain exercisable for three months following the termination of service. However, in no event may an option be exercised later than the expiration of its term. Subject to the provisions of our 2014 Plan, the administrator determines the other terms of options.

Stock appreciation rights. Stock appreciation rights may be granted under our 2014 Plan. Stock appreciation rights allow the recipient to receive the appreciation in the fair market value of our common stock between the exercise date and the date of grant. Stock appreciation rights may not have a term exceeding 10 years. After the termination of service of an employee, director or consultant, he or she may exercise his or her stock appreciation right for the period of time stated in his or her option agreement. However, in no event may a stock appreciation right be exercised later than the expiration of its term. Subject to the provisions of our 2014 Plan, the administrator determines the other terms of stock appreciation rights, including when such rights become exercisable and whether to pay any increased appreciation in cash or with shares of our common stock, or a combination thereof, except that the per share exercise price for the shares to be issued pursuant to the exercise of a stock appreciation right will be no less than 100% of the fair market value per share on the date of grant.

Restricted stock. Restricted stock may be granted under our 2014 Plan. Restricted stock awards are grants of shares of our common stock that vest in accordance with terms and conditions established by the administrator. The administrator will determine the number of shares of restricted stock granted to any employee, director or consultant and, subject to the provisions of our 2014 Plan, will determine the terms and conditions of such awards. The administrator may impose whatever conditions for lapse of the restriction on the shares it determines to be appropriate (for example, the administrator may set restrictions based on the achievement of specific performance goals or continued service to us); provided, however, that the administrator, in its sole discretion, may accelerate the time at which any restrictions will lapse or be removed. Recipients of restricted stock awards generally will have voting and dividend rights with respect to such shares upon grant without regard to the restriction, unless the administrator provides otherwise. Shares of restricted stock as to which the restrictions have not lapsed are subject to our right of repurchase or forfeiture.

Restricted stock units. Restricted stock units may be granted under our 2014 Plan. Restricted stock units are bookkeeping entries representing an amount equal to the fair market value of one share of our common stock. Subject to the provisions of our 2014 Plan, the administrator will determine the terms and conditions of restricted stock units, including the vesting criteria (which may include accomplishing specified performance criteria or continued service to us) and the form and timing of payment. Notwithstanding the foregoing, the administrator, in its sole discretion, may accelerate the time at which any restricted stock units will vest.

Performance units and performance shares. Performance units and performance shares may be granted under our 2014 Plan. Performance units and performance shares are awards that will result in a payment to a participant only if performance goals established by the administrator are achieved or the awards otherwise vest. The administrator will establish organizational or individual performance goals or other vesting criteria in its discretion, which, depending on the extent to which they are met, will determine the number and/or the value of performance units and performance shares to be paid out to participants. After the grant of a performance unit or performance share, the administrator, in its sole discretion, may reduce or waive any performance criteria or other vesting provisions for such performance units or performance shares. Performance units shall have an initial dollar value established by the administrator prior to the grant date. Performance shares shall have an initial value equal to the fair market value of our common stock on the grant date. The administrator, in its sole discretion, may pay earned performance units or performance shares in the form of cash, in shares or in some combination

Non-employee directors. Our 2014 Plan provides that all non-employee directors are eligible to receive all types of awards (except for incentive stock options) under the 2014 Plan. Our 2014 Plan provides that in any

given fiscal year, a non-employee director may not receive under the 2014 Plan awards having a grant date fair value greater than $450,000, increased to $600,000 in connection with his or her initial service, in each case, as grant fair value is determined under generally accepted accounting principles. Our 2014 Plan further provides that, in the event of a merger or change in control, as defined in our 2014 Plan, each outstanding equity award granted under our 2014 Plan that is held by a non-employee director will fully vest, all restrictions on the shares subject to such award will lapse, and with respect to awards with performance-based vesting, all performance goals or other vesting criteria will be deemed achieved at 100% of target levels, and all of the shares subject to such award will become fully exercisable, if applicable.

Non-transferability of awards. Unless the administrator provides otherwise, our 2014 Plan generally does not allow for the transfer of awards and only the recipient of an award may exercise an award during his or her lifetime.

Certain adjustments. In the event of certain changes in our capitalization, to prevent diminution or enlargement of the benefits or potential benefits available under our 2014 Plan, the administrator will adjust the number and class of shares that may be delivered under our 2014 Plan and/or the number, class and price of shares covered by each outstanding award and the numerical share limits set forth in our 2014 Plan. In the event of our proposed liquidation or dissolution, the administrator will notify participants as soon as practicable and all awards will terminate immediately prior to the consummation of such proposed transaction.

Merger or change in control. Our 2014 Plan provides that in the event of a merger or change in control, as defined under the 2014 Plan, each outstanding award will be treated as the administrator determines, except that if a successor corporation or its parent or subsidiary does not assume or substitute an equivalent award for any outstanding award, then such award will fully vest, all restrictions on the shares subject to such award will lapse, all performance goals or other vesting criteria applicable to the shares subject to such award will be deemed achieved at 100% of target levels and all of the shares subject to such award will become fully exercisable, if applicable, for a specified period prior to the transaction. The award will then terminate upon the expiration of the specified period of time.

Amendment, termination. The administrator will have the authority to amend, suspend or terminate the 2014 Plan provided such action will not impair the existing rights of any participant. Our 2014 Plan will automatically terminate in 2024, unless we terminate it sooner.

2014 Employee Stock Purchase Plan

Our board of directors adopted, and our stockholders approved, a 2014 Employee Stock Purchase Plan, or ESPP, in connection with our initial public offering.

The ESPP includes a component that is intended to qualify as an employee stock purchase plan under Section 423 of the Internal Revenue Code of 1986, as amended, or the 423 Component, and a component that does not comply with Section 423, or the Non-423 Component. For purposes of this disclosure, a reference to the ESPP will mean the 423 Component. Unless determined otherwise by the administrator, each of our non-U.S. subsidiaries will participate in a separate offering under the Non-423 Component.

Authorized shares. A total of 380,000 shares of our common stock have been made available for sale. In addition, our ESPP provides for annual increases in the number of shares available for issuance under the ESPP on the first day of each fiscal year beginning in fiscal 2015, equal to the least of:

1.5% of the outstanding shares of our common stock on the last day of the previous fiscal year;

800,000 shares; or

such other amount as may be determined by our board of directors.

Under this provision, 317,599 shares were added to the ESPP s share reserve effective January 1, 2015.

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Plan administration. Our board of directors or a committee appointed by our board of directors administers the ESPP. Our board of directors has appointed our compensation committee to administer the ESPP. The administrator has authority to administer the plan, including but not limited to, full and exclusive authority to interpret the terms of the ESPP, determine eligibility to participate subject to the conditions of our ESPP as described below, and to establish procedures for plan administration necessary for the administration of the ESPP, including creating sub-plans.

Eligibility. Generally, all of our employees will be eligible to participate if they are employed by us, or any participating subsidiary, for at least 20 hours per week and more than five months in any calendar year. However, an employee may not be granted an option to purchase stock under the ESPP if such employee:

- immediately after the grant would own stock constituting 5% or more of the total combined voting power or value of all classes of our capital stock; or
- holds rights to purchase stock under all of our employee stock purchase plans that accrue at a rate that exceeds $25,000 worth of stock for each calendar year in which the option is outstanding.

Offering periods. Our ESPP is intended to qualify under Section 423 of the Code, and provides for 24-month offering periods, which generally will include six-month purchase periods. The offering periods generally start on the first trading day on or after June 1 and December 1 of each year, except that the first offering period commenced on the first trading day following the effective date of our initial public offering. The administrator may, in its discretion, modify the terms of future offering periods.

Payroll deductions. Our ESPP will permit participants to purchase common stock through payroll deductions of up to 15% of their eligible compensation, which includes a participant s base straight time gross earnings, but exclusive of payments for incentive compensation, payment for overtime and shift premiums, equity compensation income, bonuses and other similar compensation. A participant may purchase a maximum of 2,500 shares during a purchase period.

Exercise of option. Amounts deducted and accumulated by the participant are used to purchase shares of our common stock at the end of each six-month purchase period. The purchase price of the shares will be 85% of the lower of the fair market value of our common stock on the first trading day of each offering period or on the exercise date. Participants may end their participation at any time during an offering period, and will be paid their accrued payroll deductions that have not yet been used to purchase shares of common stock. Participation ends automatically upon termination of employment with us.

Non-transferability. A participant may not transfer rights granted under our ESPP other than by will, the laws of descent and distribution, or as otherwise provided under our ESPP.

Merger or change in control. In the event of our merger or change in control, as defined under the ESPP, a successor corporation may assume or substitute for each outstanding option. If the successor corporation refuses to assume or substitute for the option, the offering period then in progress will be shortened, and a new exercise date will be set. The administrator will notify each participant that the exercise date has been changed and that the participant s option will be exercised automatically on the new exercise date unless prior to such date the participant has withdrawn from the offering period.

Amendment, termination. Our ESPP will automatically terminate in 2034, unless we terminate it sooner. The administrator has the authority to amend, suspend or terminate our ESPP at any time.

Amended and Restated 2010 Equity Incentive Plan

Our board of directors adopted, and our stockholders approved, our 2010 Equity Incentive Plan, or the 2010 Plan, in May 2010.

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Authorized shares. We terminated our 2010 Plan in connection with our initial public offering, and, accordingly, no shares are available for issuance under the 2010 Plan. Notwithstanding the foregoing, the 2010 Plan will continue to govern outstanding awards granted thereunder. As of September 30, 2014, options to purchase 2,054,710 shares of common stock remained outstanding under the 2010 Plan.

Plan administration. Our board of directors or a committee of our board (the administrator) administers our 2010 Plan. The administrator has the power to determine the recipients of awards; to determine the terms of the awards; to institute and determine the terms and conditions of a program under which (i) outstanding stock awards are surrendered or cancelled in exchange for stock awards (which may have different exercise prices and terms, be of a different type and/or be issued under another equity plan) and/or cash, (ii) participants have the opportunity to transfer stock awards to a financial institution or other person or entity selected by the administrator and/or (iii) the exercise price of an outstanding stock award is reduced or increased; to construe and interpret or correct any defects in the 2010 Plan and any awards; and to exercise such powers and perform such acts consistent with the provisions of the 2010 Plan as the board or committee deems necessary or expedient to promote the best interests of us or our stockholders.

Stock options. Under the 2010 Plan, the administrator had the power to grant options. The exercise price of nonstatutory stock options granted under our 2010 Plan had to be at least equal to 85% of the fair market value of our common stock on the date of grant, as determined by our board of directors. The exercise price of incentive stock options granted under our 2010 Plan had to be at least equal to 100% of the fair market value of our common stock on the date of grant, as determined by our board of directors. Notwithstanding the foregoing, options could be granted with a per share exercise price less than the values described in the two preceding sentences pursuant to a transaction described in, and in a manner consistent with, Section 424(a) of the Code. The term of an incentive stock option could not exceed 10 years, except that with respect to any participant who owned 10% of the voting power of all classes of our outstanding stock as of the grant date, the term could not exceed 5 years and the exercise price had to be at least equal to 110% of the fair market value on the grant date. The 2010 Plan administrator determines the terms and conditions of options.

After termination of an employee, director or consultant, he or she may exercise his or her option for the period of time stated in the option agreement. Generally, if termination is due to death, it is expected that the option will remain exercisable for 18 months, and if termination is due to disability, it is expected that the option will remain exercisable for 12 months. In all other cases, it is expected that the option will generally remain exercisable for three months. However, an option generally may not be exercised later than the expiration of its term.

Restricted stock and stock bonuses. Under the 2010 Plan, the administrator had the power to grant restricted stock awards. Restricted stock awards are shares of our common stock that vest in accordance with terms and conditions established by the administrator. The administrator may impose whatever conditions to vesting it determines to be appropriate. Shares of restricted stock that do not vest are subject to our right of repurchase or forfeiture. The purchase price of restricted stock awards could not be less than 85% of the fair market value of our common stock on the date of grant, as determined by the board of directors, provided that restricted shares awarded as a stock bonus did not require the payment of a cash purchase price.

Non-transferability of awards. Our 2010 Plan does not allow for the transfer of awards except by will or by the laws of descent and distribution, and awards are exercisable (as applicable) during the lifetime of a participant only by the participant, provided that options may also be transferred as permitted by Section 260.140.41(d) of Title 10 of the California Code of Regulations.

Corporate transaction. Our 2010 Plan provides that in the event of a corporate transaction, as defined in the 2010 Plan, the surviving or acquiring corporation may assume or substitute an equivalent award for each outstanding award, and any reacquisition or repurchase rights held by us in respect of the common stock issued pursuant to the award may be assigned by us to the surviving or acquiring corporation in connection with such corporate transaction. In the event that any surviving corporation or acquiring corporation does not assume or

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continue any or all outstanding awards, then with respect to awards that are not assumed, continued or substituted, such awards shall terminate if not exercised (if applicable) at or prior to the corporate transaction, and any reacquisition or repurchase rights held by us with respect to such awards that are held by participants whose continuous service to us has not terminated shall lapse.

The 2010 Plan provides that in the event of a change in control, awards held by participants whose continuous service to us has not terminated prior to the change in control may be subject to additional acceleration of vesting if such acceleration is provided for in the applicable award agreement. In the absence of any such acceleration provision, no such acceleration shall occur.

Certain adjustments. If any change is made in, or any event occurs with respect to, our common stock without our receipt of consideration through a merger, consolidation, reorganization, recapitalization, reincorporation, stock dividend, dividend in property other than cash, stock split, liquidating dividend, combination of shares, exchange of shares, change in corporate structure or other transaction, the 2010 Plan will be appropriately adjusted by the administrator as to the class and maximum number of securities subject to the 2010 Plan and the class, number of securities and price per share of common stock subject to outstanding awards under the 2010 Plan.

Dissolution or liquidation. In the event of our dissolution or liquidation, all outstanding awards shall terminate immediately prior to the completion of such dissolution or liquidation, and shares of common stock subject to any repurchase option in our favor may be repurchased by us, regardless of whether or not the applicable participant s continuous service with us has terminated.

Amendment, termination. Our board of directors has the authority to amend, suspend or terminate the 2010 Equity Incentive Plan provided such action does not impair the rights of any participant with respect to an outstanding stock award. Our 2010 Plan terminated in connection with our initial public offering and no further awards will be granted thereunder. Notwithstanding the foregoing, outstanding options granted under the 2010 Plan will continue to be governed by the 2010 Plan.

401(k) Plan

We maintain a tax-qualified retirement plan that provides eligible employees with an opportunity to save for retirement on a tax advantaged basis. All participants interests in our matching and profit sharing contributions, if any, vest pursuant to a six-year graded vesting schedule from the time of contribution. In 2013, we made no matching or profits sharing contributions into the 401(k) plan. Pre-tax contributions are allocated to each participant s individual account and are then invested in selected investment alternatives according to the participants directions. The 401(k) plan is intended to qualify under Sections 401(a) and 501(a) of the Code. As a tax-qualified retirement plan, contributions to the 401(k) plan and earnings on those contributions are not taxable to the employees until distributed from the 401(k) plan, and all contributions are deductible by us when made.

Limitations on Liability and Indemnification Matters

Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, and may indemnify our employees and other agents, to the fullest extent permitted by Delaware law. Delaware law prohibits our amended and restated certificate of incorporation from limiting the liability of our directors for the following:

any breach of the director s duty of loyalty to us or to our stockholders;

acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;

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unlawful payment of dividends or unlawful stock repurchases or redemptions; and

any transaction from which the director derived an improper personal benefit.

If Delaware law is amended to authorize corporate action further eliminating or limiting the personal liability of a director, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law, as so amended. Our amended and restated certificate of incorporation does not eliminate a director s duty of care and, in appropriate circumstances, equitable remedies, such as injunctive or other forms of non-monetary relief, remain available under Delaware law. This provision also does not affect a director s responsibilities under any other laws, such as the federal securities laws or other state or federal laws. Under our amended and restated bylaws, we are also empowered to purchase insurance on behalf of any person whom we are required or permitted to indemnify.

In addition to the indemnification required in our amended and restated certificate of incorporation and amended and restated bylaws, we have entered into an indemnification agreement with each member of our board of directors and each of our officers. These agreements provide for the indemnification of our directors and officers for certain expenses and liabilities incurred in connection with any action, suit, proceeding or alternative dispute resolution mechanism, or hearing, inquiry or investigation that may lead to the foregoing, to which they are a party, or are threatened to be made a party, by reason of the fact that they are or were a director, officer, employee, agent or fiduciary of our company, or any of our subsidiaries, by reason of any action or inaction by them while serving as an officer, director, agent or fiduciary, or by reason of the fact that they were serving at our request as a director, officer, employee, agent or fiduciary of another entity. In the case of an action or proceeding by or in the right of our company or any of our subsidiaries, no indemnification will be provided for any claim where a court determines that the indemnified party is prohibited from receiving indemnification. We believe that these charter and bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duties. They may also reduce the likelihood of derivative litigation against directors and officers, even though an action, if successful, might benefit us and our stockholders. Moreover, a stockholder s investment may be harmed to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions. Insofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act, and is, therefore, unenforceable. There is no pending litigation or proceeding naming any of our directors or officers as to which indemnification is being sought, nor are we aware of any pending or threatened litigation that may result in claims for indemnification by any director or officer.

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CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

In addition to the director and executive officer compensation arrangements and indemnification arrangements discussed above in the sections titled Management and Executive Compensation and the registration rights described in the section titled Description of Capital Stock Registration Rights, the following is a description of each transaction since January 1, 2012 and each currently proposed transaction in which:

- we have been or are to be a participant;
- the amount involved exceeded or exceeds $120,000; and
- any of our directors, executive officers or, to our knowledge, beneficial owners of more than 5% of our capital stock, or any immediate family member of or person sharing the household with any of these individuals, had or will have a direct or indirect material interest.

Preferred Stock Financings and Convertible Note Financing

Series D Preferred Stock Financing

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 consideration of approximately $49.3 million. The participants in this preferred stock financing included certain of our officers, directors and holders of more than 5% of our capital stock or entities affiliated with them and certain other investors. The following table presents the aggregate number of shares of series D convertible preferred stock issued to these related parties in this preferred stock financing:

Name of Stockholder	Affiliated Director(s) or Officer(s)	Number of Series D Shares	Total Purchase Price($)
OrbiMed Private Investment IV, LP	Chau Q. Khuong	378,039	$ 4,519,236
Novo A/S	Peter Bisgaard	348,041	4,160,626
TPG Biotechnology Partners III, L.P.	Heather Preston, M.D.	348,041	4,160,626
Domain Associates[1]	Brian Dovey	188,214	2,250,000
RiverVest Venture Partners[2]	John P. McKearn, Ph.D.	179,426	2,144,946
Avalon Ventures[3]	Jay Lichter, Ph.D.	136,770	1,635,010
Vickie Capps	Vickie Capps	20,912	250,000
Harris Family Trust dated July 27, 2007	Jeffrey Harris, M.D., Ph.D.[4]	2,091	25,000
The Weber Trust Dated March 9, 2005	David A. Weber, Ph.D.	1,254	15,000

(1) Consists of 186,828 shares of series D convertible preferred stock issued to Domain Partners VIII, L.P. and 1,386 shares of series D convertible preferred stock issued to DP VIII Associates, L.P.

(2) Consists of 141,101 shares of series D convertible preferred stock issued to RiverVest Venture Fund II, L.P. and 38,325 shares of series D convertible preferred stock issued to RiverVest Venture Fund II (Ohio), L.P.

(3) Consists of 136,770 shares of series D convertible preferred stock issued to Avalon Ventures X, L.P.
(4) Dr. Harris resigned from our board of directors in March 2014.

Series C Preferred Stock Financing

Between August 26, 2013 and December 17, 2013, we sold an aggregate of 7,040,026 shares of series C convertible preferred stock at a per share purchase price of $8.79 pursuant to a series C preferred stock purchase agreement for aggregate consideration of approximately $61.9 million, which such amounts include the conversion of the secured convertible promissory notes described below. Participants in this preferred stock financing included certain of our officers, directors and holders of more than 5% of our capital stock or

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entities affiliated with them and certain other investors, all of which are collectively referred to herein as the Series C Investors. The following table presents the aggregate number of shares issued to these related parties in this preferred stock financing:

Name of Stockholder	Affiliated Director(s) or Officer(s)	Number of Series C Shares	Total Purchase Price($)[4]
OrbiMed Private Investment IV, LP	Chau Q. Khuong	1,706,484	$ 15,000,000
Novo A/S	Peter Bisgaard	1,131,436	9,945,332
TPG Biotechnology Partners III, L.P.	Heather Preston, M.D.	1,131,436	9,945,332
Avalon Ventures[1]	Jay Lichter, Ph.D.	1,053,519	9,260,442
Domain Associates[2]	Brian Dovey	932,345	8,195,332
RiverVest Venture Partners[3]	John P. McKearn, Ph.D.	612,083	5,380,221
The Weber Trust Dated March 9, 2005	David A. Weber, Ph.D.	3,445	30,288
Harris Family Trust dated July 27, 2007	Jeffrey Harris, M.D. Ph.D.[5]	2,844	25,000

(1) Consists of 568,828 shares of series C convertible preferred stock issued to Avalon Ventures X, L.P. and 484,691 shares of series C convertible preferred stock issued to Avalon Ventures VIII, L.P.
(2) Consists of 925,479 shares of series C convertible preferred stock issued to Domain Partners VIII, L.P. and 6,866 shares of series C convertible preferred stock issued to DP VIII Associates, L.P.
(3) Consists of 481,342 shares of series C convertible preferred stock issued to RiverVest Venture Fund II, L.P. and 130,741 shares of series C convertible preferred stock issued to RiverVest Venture Fund II (Ohio), L.P.
(4) In some cases, all or a portion of the purchase price was accounted for by conversion of promissory notes issued as part of the 2012-2013 bridge financing.
(5) Dr. Harris resigned from our board of directors in March 2014.

2012-2013 Bridge Financing

Between August 23, 2012 and January 22, 2013, we sold an aggregate of $15.0 million in secured convertible promissory notes to certain of the Series C Investors. On August 26, 2013, these secured convertible promissory notes converted into 1,818,191 shares of our series C convertible preferred stock pursuant to the terms of the notes. In connection with the issuance of these secured convertible promissory notes, we issued warrants exercisable for an aggregate of 341,404 shares of our series C convertible preferred stock at an exercise price of $8.79 per share to certain of the Series C Investors. The following table presents the aggregate amount of securities issued to our officers, directors and holders of more than 5% of our capital stock or entities affiliated with them in this bridge financing:

Name of Stockholder	Affiliated Director(s) or Officer(s)	Aggregate Principal Amount of Secured Convertible Promissory Notes($)	Number of Shares of Series C Convertible Preferred Stock Underlying Warrants
Avalon Ventures VIII, L.P.	Jay Lichter, Ph.D.	$ 4,000,000	91,011

Novo A/S	Peter Bisgaard	3,000,000	68,259
TPG Biotechnology Partners III, L.P.	Heather Preston, M.D.	3,000,000	68,259
Domain Associates[1]	Brian Dovey	3,000,000	68,257
RiverVest Venture Partners[2]	John P. McKearn, Ph.D.	2,000,000	45,505
The Weber Trust Dated March 9, 2005	David A. Weber, Ph.D.	4,999	113

(1) Consists of $2,977,903 of secured convertible promissory notes issued to Domain Partners VIII, L.P. and $22,097 of secured convertible promissory notes issued to DP VIII Associates, L.P. Consists of 67,755 shares of series C convertible preferred stock underlying warrants held by Domain Partners VIII, L.P. and 502 shares of series C convertible preferred stock underlying warrants held by DP VIII Associates, L.P.

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(2) Consists of $1,572,800 of secured convertible promissory notes issued to RiverVest Venture Fund II, L.P. and $427,200 of secured convertible promissory notes issued to RiverVest Venture Fund II (Ohio), L.P. Consists of 35,785 shares of series C convertible preferred stock underlying warrants held by RiverVest Venture Fund II, L.P. and 9,720 shares of series C convertible preferred stock underlying warrants held by RiverVest Venture Fund II (Ohio), L.P.

Investors Rights Agreement

In connection with our sale and issuance of series D convertible preferred stock in April 2014, we entered into a third amended and restated investors rights agreement with the holders of our convertible preferred stock, including all of the holders of more than 5% of our capital stock or entities affiliated with them and with which certain of our directors are affiliated, Vickie Capps, a member of our board of directors, and an entity affiliated with David A. Weber, Ph.D., a member of our board directors and our President and Chief Executive Officer. This agreement provides, among other things, for certain registration rights, information rights and rights of first refusal. For a more detailed description of the registration rights provided for under this agreement, see the section titled Description of Capital Stock Registration Rights .

Stockholders Agreement

In connection with our sale and issuance of series D convertible preferred stock in April 2014, we entered into a third amended and restated stockholders agreement with certain of the holders of our common stock, the holders of our convertible preferred stock, including all of the holders of more than 5% of our capital stock or entities affiliated with them and with which certain of our directors are affiliated, Vickie Capps, a member of our board of directors, and an entity affiliated with David A. Weber, Ph.D., a member of our board directors and our President and Chief Executive Officer. The parties to the stockholders agreement agreed, subject to certain conditions, to vote the shares of our capital stock held by them so as to elect the following individuals as directors: (1) the person serving as our chief executive officer; (2) one nominee designated by Avalon Ventures VIII, L.P. and its affiliates, currently Jay Lichter, Ph.D.; (3) one nominee designated by Novo A/S and its affiliates, currently Peter Bisgaard; (4) one nominee designated by RiverVest Venture Fund II L.P., RiverVest Venture Fund II (OHIO) L.P., and their affiliates, currently John P. McKearn, Ph.D.; (5) one nominee designated by TPG Biotechnology Partners III, L.P. and its affiliates, currently Heather Preston, M.D.; (6) one nominee designated by Domain Partners VIII, L.P., DP VIII Associates, and their affiliates, currently Brian Dovey; and (7) one nominee designated by OrbiMed Private Investments IV, LP and its affiliates, currently Chau Q. Khuong. In addition, the parties to the stockholders agreement agreed to vote their shares to elect one independent director who is designated by at least 75% of our outstanding convertible preferred stock on an as-converted basis, excluding shares of series A convertible preferred stock and series C convertible preferred stock issuable upon exercise of outstanding warrants, currently Vickie Capps. Further, the stockholders agreement contains certain other rights such as a drag-along voting provision and rights of first refusal and co-sale. Upon the consummation of our initial public offering, the obligations of the parties to the stockholders agreement to vote their shares so as to elect these nominees, as well as the other rights and obligations under this agreement, terminated and none of our stockholders have any special rights regarding the nomination, election or designation of members of our board of directors.

Indemnification of Officers and Directors

We have entered, and intend to continue to enter, into separate indemnification agreements with each of our directors and executive officers, in addition to the indemnification provided for in our amended and restated certificate of incorporation and amended and restated bylaws. The indemnification agreements and our amended restated certificate of incorporation and amended and restated bylaws require us to indemnify our directors, executive officers and certain controlling persons to the fullest extent permitted by Delaware law. See the section titled Executive

Compensation Limitations on Liability and Indemnification Matters above.

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Arrangements with Avalon-Affiliated Entities

In 2012, we made payments of approximately $0.1 million in the aggregate to, and received payments of $0.1 million in the aggregate from, entities affiliated with Avalon Ventures, an owner of more than 5% of our capital stock, in connection with various arrangements pursuant to which we and the Avalon-affiliated entities shared common services, such as accounting and finance support, and shared facilities. In 2013, we made payments of approximately $30,000 in the aggregate to, and received payments of $0.1 million in the aggregate from, such entities in connection with such arrangements. There are no resource sharing arrangements currently in place with such entities. Jay Lichter, Ph.D., a member of our board of directors, is a managing director at Avalon Ventures.

Participation in Initial Public Offering

Certain of our existing stockholders, who are affiliated with members of our board of directors, purchased shares in our initial public offering, at the initial public offering price. The following table presents the number of shares of common stock issued and sold to our affiliated entities at the initial public offering.

Purchaser	Affiliated Director(s)	Shares of Common Stock
Novo A/S	Peter Bisgaard	171,875
OrbiMed Private Investment IV, LP	Chau Q. Khuong	171,875
TPG Biotechnology Partners III, L.P.	Heather Preston, M.D.	171,875
Avalon Ventures X, L.P.	Jay Lichter, Ph.D.	109,375

Related-Person Transactions Policy

Our audit committee has the primary responsibility for reviewing and approving or disapproving related party transactions, which, as defined in our written related party transactions policy, are transactions in which we participate and the aggregate amount involved exceeds or may be expected to exceed $120,000, and in which a related person has or will have a direct or indirect material interest. For purposes of this policy, a related person will be defined as a director, executive officer, or nominee for director, in each case at any time since the beginning of the most recently completed year, and their immediate family members, or any person or entity who is or will be, at the time a transaction, arrangement or relationship occurs or exists, a greater than 5% beneficial owner of our common stock, and their immediate family members. Our audit committee charter provides that the audit committee shall review and approve or disapprove any related party transactions.

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PRINCIPAL STOCKHOLDERS

The following table sets forth the beneficial ownership of our common stock as of December 31, 2014 by:

- each person, or group of affiliated persons, who we know to beneficially own more than 5% of our common stock;
- each of our named executive officers;
- each of our directors; and
- all of our executive officers and directors as a group.

The percentage ownership information prior to the offering shown in the table is based on an aggregate of 21,173,270 shares of our common stock outstanding as of December 31, 2014. The percentage ownership information after the offering assumes the issuance of shares of common stock in this offering (and no exercise of the underwriters option to purchase additional shares).

We have determined beneficial ownership in accordance with the rules of the SEC. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities. In addition, the rules include shares of common stock issuable pursuant to the exercise of stock options and warrants that are either immediately exercisable or exercisable on or before March 1, 2015, which is 60 days after December 31, 2014. These shares are deemed to be outstanding and beneficially owned by the person holding those options and warrants for the purpose of computing the percentage ownership of that person, but they are not treated as outstanding for the purpose of computing the percentage ownership of any other person. Unless otherwise indicated, the persons or entities identified in this table have sole voting and investment power with respect to all shares shown as beneficially owned by them, subject to applicable community property laws.

Unless otherwise noted below, the address of each of the individuals and entities named in the table below is c/o Otonomy, Inc., 6275 Nancy Ridge Drive, Suite 100, San Diego, California 92121. Beneficial ownership representing less than 1% is denoted with an asterisk (*).

Name of Beneficial Owner	Number of Shares Beneficially Owned	Percent of Shares Beneficially Owned	
		Before the Offering	After the Offering
5% Stockholders:			
Entities affiliated with Avalon Ventures[1]	2,406,212	11.3%	
OrbiMed Private Investments IV, LP[2]	2,256,398	10.7%	
Novo A/S[3]	2,175,025	10.3%	
TPG Biotechnology Partners III, L.P.[4]	2,159,335	10.2%	
Entities affiliated with Domain Associates[5]	1,591,038	7.5%	

Entities affiliated with RiverVest Venture Partners[6]	1,009,888	4.8%
Named Executive Officers and Directors:		
David A. Weber, Ph.D.[7]	682,612	3.1%
Paul E. Cayer[8]	110,609	*
Anthony J. Yost[9]		*
Peter Bisgaard[10]		
Vickie Capps[11]	42,242	*
Brian Dovey[12]	1,591,038	7.5%
Chau Q. Khuong[13]	2,256,398	10.7%
Jay Lichter, Ph.D.[14]	2,406,212	11.3%

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Name of Beneficial Owner	Number of Shares Beneficially Owned	Percent of Shares Beneficially Owned Before the Offering	Percent of Shares Beneficially Owned After the Offering
John P. McKearn, Ph.D.[15]	1,009,888	4.8%	
Heather Preston, M.D.[16]			
All executive officers and directors as a group (12 persons)[17]	8,234,640	37.1%	

(1) Based on information set forth in a Schedule 13D filed with the SEC by entities affiliated with Avalon Ventures on August 28, 2014, these shares consist of (i) 141,060 shares issuable upon the exercise of warrants held by Avalon Ventures VIII, L.P. (Avalon VIII), (ii) 1,450,179 shares held by Avalon VIII and (iii) 814,973 shares held by Avalon Ventures X, L.P. (Avalon X). Kevin Kinsella, Stephen Tomlin, Richard Levandov, Braden Bohrmann, Douglas Downs and Jay Lichter, Ph.D. are managing directors of Avalon X and Avalon VIII and share voting and dispositive power over the shares held by each entity. Each disclaims beneficial ownership of the securities reported herein except to the extent of his pecuniary interest therein. The address for these entities is 1134 Kline Street, La Jolla, California 92037.

(2) Based on information set forth in a Schedule 13D filed with the SEC by individuals and entities affiliated with OrbiMed Private Investments IV, LP (OrbiMed) on August 22, 2014, these shares consist of 2,256,398 shares held by OrbiMed. OrbiMed Capital GPV LLC (OrbiMed Capital) is the sole general partner of OrbiMed. OrbiMed Advisors LLC (OrbiMed Advisors) is the managing member of OrbiMed Capital. OrbiMed Capital and OrbiMed Advisors may be deemed to have beneficial ownership of the shares held by OrbiMed. Samuel D. Islay is the managing member of and owner of a controlling interest in OrbiMed Advisors and as such may be deemed to have beneficial ownership of the shares held by OrbiMed. Chau Khuong, one of our directors, is employed as a Private Equity Partner at OrbiMed Advisors. Each of OrbiMed Capital, OrbiMed Advisors, Mr. Islay and Mr. Khuong disclaims beneficial ownership of the shares held by OrbiMed except to the extent of its or his pecuniary interest therein, if any. The address for these entities is 601 Lexington Avenue, 54th floor, New York, New York 10022.

(3) Based on information set forth in a Schedule 13G filed with the SEC by Novo A/S, a Danish limited liability company (Novo), on August 28, 2014, these shares consist of 2,175,025 shares held by Novo. The board of directors of Novo consists of Sten Scheibye, Göran Ando, Jeppe Christiansen, Steen Riisgaard and Per Wold-Olsen, who have shared investment and voting control with respect to the shares held by Novo and may exercise such control only with the support of a majority of the members of the Novo board of directors. No individual member of the Novo board of directors is deemed to hold any beneficial ownership or reportable pecuniary interest in the shares held by Novo. Peter Bisgaard, one of our directors, is employed as a partner of Novo Ventures (US) Inc., a consultant to Novo, and is not deemed to beneficially own the shares held by Novo. The address for Novo is Tuborg Havnevej 19, 2900 Hellerup, Denmark.

(4) Based on information set forth in a Form 4 filed with the SEC by individuals and entities affiliated with TPG Biotechnology Partners III, L.P. (TPG Biotech) on August 19, 2014, these shares consist of 2,159,335 shares held TPG Biotech. The general partner of TPG Biotech is TPG Biotechnology GenPar III, L.P., a Delaware limited partnership, whose general partner is TPG Biotechnology GenPar III Advisors, LLC, a Delaware limited liability company, whose sole member is TPG Holdings I, L.P., a Delaware limited partnership, whose general partner is TPG Holdings I-A, LLC, a Delaware limited liability company, whose sole member is TPG Group Holdings (SBS), L.P., a Delaware limited partnership, whose general partner is TPG Group Holdings (SBS) Advisors, Inc., a Delaware corporation. David Bonderman and James G. Coulter are officers and sole stockholders of TPG Group Holdings (SBS) Advisors, Inc. and may therefore be deemed to be the beneficial owners of the securities held by the TPG Biotech. Messrs. Bonderman, Coulter disclaim beneficial ownership of the securities reported herein except to the extent of their pecuniary interest therein. The address of each of TPG Group Holdings (SBS) Advisors, Inc. and Messrs. Bonderman and Coulter is c/o TPG Global, LLC, 301 Commerce Street, Suite 3300,

Fort Worth, Texas 76102.

(5) Based on information set forth in Forms 4 filed with the SEC by individuals and entities affiliated with Domain Associates on August 18, 2014, these shares consist of (i) 1,579,323 shares held by Domain Partners VIII, L.P. (Domain) and (ii) 11,715 shares held by DP VIII Associates, L.P. (DP). One Palmer Square Associates VIII, LLC (One Palmer Square) is the general partner of Domain and DP, and the Managing Members of One Palmer Square share voting and investment power with respect to the shares held by Domain and DP. Brian Dovey, one of our directors, James C. Blair, Jesse I. Treu, Kathleen K. Schoemaker, Brian K. Halak and Nicole Vitullo (collectively, the Managing Members) are each Managing Members of One Palmer Square. The Managing Members disclaim beneficial ownership except to the extent of their pecuniary interest therein. The address of these entities is One Palmer Square, Suite 515, Princeton, New Jersey 08542.

(6) Consists of (i) 794,177 shares held by RiverVest Venture Fund II, L.P. (RiverVest) and (ii) 215,711 shares held by RiverVest Venture Fund II (Ohio), L.P. (RiverVest (Ohio)). John P. McKearn, Ph.D., one of our directors, is an Authorized Person of RiverVest Venture Partners II, LLC (RiverVest Venture), the general partner of RiverVest Partners II, L.P. RiverVest Partners II, L.P. is the sole member of RiverVest Venture Partners II (Ohio), LLC, the general partner of RiverVest (Ohio). RiverVest Partners II, L.P. is also the general partner of RiverVest. As an Authorized Person of RiverVest Venture and RiverVest 3x5 Special Opportunity Managers, LLC, Dr. McKearn may be deemed to share dispositive voting and investment power with respect to the shares held by such entities. Dr. McKearn disclaims beneficial ownership of such shares except to the extent of his pecuniary interest therein. The address of these entities is 7733 Forsyth Boulevard, Suite 1650, St. Louis, Missouri 63105.

(7) Consists of (i) 660,736 shares held by Dr. Weber issuable upon the exercise of options that are exercisable within 60 days of December 31, 2014, of which 283,874 are fully vested as of December 31, 2014, (ii) 4,812 shares held by The Weber Trust Dated March 9, 2005, for which Dr. Weber serves as a trustee and (iii) 17,064 shares held of record by Dr. Weber.

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(8) Consists of (i) 103,499 shares issuable upon the exercise of options that are exercisable within 60 days of December 31, 2014, 93,824 of which fully vested as of December 31, 2014 and (ii) 7,110 shares.
(9) No shares are beneficially owned as of December 31, 2014.
(10) Mr. Bisgaard is employed as a partner of Novo Ventures (US) Inc., a consultant to Novo A/S, and is not deemed to beneficially own the shares held by Novo A/S.
(11) Consists of 42,242 shares, of which 13,627 shares may be repurchased by us at the original purchase price as of December 31, 2014.
(12) Consists of the shares listed in footnote (5) above, which are held by entities affiliated with Domain Associates. Mr. Dovey, one of our directors, shares voting and investment power with respect to these shares.
(13) Consists of the shares listed in footnote (2) above, which are held by OrbiMed. Mr. Khuong, one of our directors, is a Private Equity Partner at OrbiMed Advisors, the managing member of the general partner of OrbiMed. Mr. Khuong disclaims beneficial ownership of these shares except to the extent of his pecuniary interest therein, if any.
(14) Consists of the shares listed in footnote (1) above, which are held by entities affiliated with Avalon Ventures. Dr. Lichter, one of our directors, shares voting and dispositive power with respect to these shares. Dr. Lichter disclaims beneficial ownership of these shares except to the extent of his pecuniary interest therein.
(15) Consists of the shares listed in footnote (6) above, which are held by entities affiliated with RiverVest Venture Partners. Dr. McKearn, one of our directors, may be deemed to share dispositive voting and investment power with respect to these shares. Dr. McKearn disclaims beneficial ownership of these shares except to the extent of his pecuniary interest therein.
(16) Dr. Preston, one of our directors, is a TPG Partner. Dr. Preston has no voting power or investment power over and disclaims beneficial ownership of the securities held by TPG Biotech. Dr. Preston s business address is c/o TPG Global, LLC, 301 Commerce Street, Suite 3300, Fort Worth, TX 76102.
(17) Consist of (i) 7,202,235 shares beneficially owned by our current executive officers and directors, of which 13,627 shares may be repurchased by us at the original exercise price as of December 31, 2014, (ii) 141,060 shares issuable upon the exercise of warrants and (iii) 891,345 shares issuable upon the exercise of options exercisable within 60 days of December 31, 2014, of which 477,803 are fully vested as of December 31, 2014.

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DESCRIPTION OF CAPITAL STOCK

General

The following description summarizes the most important terms of our capital stock as set forth in our amended and restated certificate of incorporation and amended and restated bylaws. This summary does not purport to be complete and is qualified in its entirety by the provisions of our amended and restated certificate of incorporation and amended and restated bylaws, copies of which have been filed as exhibits to the registration statement relating to our initial public offering. For a complete description of our capital stock, you should refer to our amended and restated certificate of incorporation, amended and restated bylaws and third amended and restated investors rights agreement, that are filed as exhibits to the registration statement relating to our initial public offering, and to the applicable provisions of Delaware law. Our authorized capital stock consists of 200,000,000 shares of common stock, $0.001 par value per share, and 10,000,000 shares of undesignated preferred stock, $0.001 par value per share.

Common Stock

Outstanding Shares

On December 31, 2014, there were 21,173,270 shares of common stock outstanding, held of record by 74 stockholders. Based on such number of shares of common stock outstanding as of December 31, 2014, and assuming the issuance by us of shares of common stock in this offering, there will be shares of common stock outstanding upon closing of this offering. Our board of directors is authorized, without stockholder approval, to issue additional shares of our capital stock.

As of December 31, 2014, there were 142,113 shares of common stock subject to outstanding warrants, and 2,707,477 shares of common stock subject to outstanding options.

Dividend Rights

Subject to preferences that may be applicable to any then outstanding convertible preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds. We have never declared or paid cash dividends on any of our capital stock and currently do not anticipate paying any cash dividends after this offering or in the foreseeable future.

Voting Rights

There are 200,000,000 shares of common stock authorized for issuance. Pursuant to our amended and restated certificate of incorporation, each holder of our common stock is entitled to one vote for each share on all matters submitted to a vote of stockholders; provided, however, that, except as otherwise required by law, holders of our common stock, as such, shall not be entitled to vote on any amendment to our amended and restated certificate of incorporation that relates solely to the terms of one or more outstanding series of preferred stock if the holders of such affected series are entitled, either separately or together with the holders of one or more other such series, to vote thereon pursuant to our amended and restated certificate of incorporation. Pursuant to our amended and restated certificate of incorporation and amended and restated bylaws, corporate actions can generally be taken by a majority of our board and/or stockholders holding a majority of our outstanding shares, except as otherwise indicated in the section entitled Anti-takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws, where certain amendments to our amended and restated certificate of incorporation and amended and restated bylaws require the vote of at least two-thirds of our then outstanding voting securities. Additionally, our stockholders do not have

cumulative voting rights in the election of directors. Accordingly, holders of a plurality of the votes cast at a meeting of stockholders will be able to elect all of the directors then standing for election.

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Right to Receive Liquidation Distributions

In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then outstanding shares of preferred stock.

Rights and Preferences

Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of our preferred stock that we may designate in the future.

Fully Paid and Nonassessable

All of our outstanding shares of common stock are, and the shares of common stock to be issued pursuant to this offering, when paid for, will be fully paid and nonassessable.

Preferred Stock

Our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of common stock. The issuance of preferred stock by us could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change of control of our company or other corporate action. No shares of preferred stock are outstanding, and we have no present plan to issue any shares of preferred stock.

Stock Options

As of December 31, 2014, there were 2,707,477 shares of our common stock issuable upon exercise of outstanding stock options, at a weighted-average exercise price of $10.20 per share.

Warrants

As of December 31, 2014, we had outstanding warrants to purchase an aggregate of 142,113 shares of our common stock at an exercise price of $14.1765 per share.

These warrants have a net exercise provision under which their holders may, in lieu of payment of the exercise price in cash, surrender the warrant and receive a net amount of shares based on the fair market value of our stock at the time of exercise of the warrants after deduction of the aggregate exercise price.

Exclusive Jurisdiction

Unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware is the sole and exclusive forum for: (i) any derivative action or proceeding brought on behalf of us; (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders; (iii) any action asserting a claim against us arising pursuant to any provision

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of the Delaware General Corporation Law or our amended and restated certificate of incorporation or amended and restated bylaws; (iv) any action to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws; or (v) any action asserting a claim against us governed by the internal affairs doctrine, in each such case, subject to said Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein. The enforceability of similar choice of forum provisions in other companies certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any action, a court could find the choice of forum provisions contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in such action.

Registration Rights

The holders of an aggregate of up to 14,079,588 shares of our common stock, including shares of common stock issuable upon the exercise of outstanding options and warrants, or their permitted transferees, are entitled to rights with respect to the registration of such shares under the Securities Act. We refer to these shares as registrable securities. These rights are provided under the terms of our third amended and restated investors rights agreement between us and the holders of registrable securities, and include demand registration rights, piggyback registration rights and Form S-3 registration rights.

These registration rights will terminate as to a given holder of registrable securities upon the earliest of (i) that date that is five years following closing of this offering or (ii) when such holder and such holder s affiliates can sell all of such holder s registrable securities during a three-month period without registration in compliance with Rule 144 of the Securities Act.

Generally, we are required to pay the registration expenses (other than underwriters and brokers discounts and commissions) in connection with the registrations described below, including the reasonable fees and disbursements of one counsel for the selling holder or holders of registrable securities. In an underwritten offering, the underwriters have the right to limit the number of shares registered by the holders of registrable securities for marketing reasons, subject to certain limitations. In connection with the completion of our initial public offering, each holder of registrable securities agreed not to sell or otherwise dispose of any securities without the prior written consent of the underwriters for a period of 180 days after the date of the final prospectus relating to our initial public offering, subject to certain terms and conditions. In addition, in connection with the completion of this offering, a substantial majority of registrable securities has agreed or will agree not to sell or otherwise dispose of any securities without the prior written consent of the underwriters for a period of 90 days after the date of this prospectus, subject to certain terms and conditions. See the section titled Shares Eligible for Future Sale Lock-Up Agreements for additional information.

Demand Registration Rights

At any time beginning 90 days after the completion of this offering, upon the written request of at least a majority of the then outstanding registrable securities that we file a registration statement under the Securities Act (provided that the anticipated aggregate offering price of such shares is greater than $5.0 million), we will be obligated to notify all holders of registrable securities of such request and to use our reasonable best efforts to register the sale of all registrable securities that holders may request to be registered. We are only obligated to file up to two registration statements which are declared or ordered effective in connection with the exercise of these demand registration rights These demand registration rights are subject to specified conditions and limitations, including the right of the underwriters to limit the number of shares included in any such registration under certain circumstances.

Piggyback Registration Rights

If we propose to register any of our securities under the Securities Act in connection with the public offering of such securities, the holders of registrable securities will be entitled to certain piggyback registration rights

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allowing such holders to include their shares in such registration, subject to certain limitations. As a result, whenever we propose to file a registration statement under the Securities Act, other than with respect to a registration related to either to the sale of securities to our employees pursuant to a stock plan, stock purchase or similar plan or a registration related to a corporate reorganization or transaction under Rule 145 of the Securities Act of registrable securities are entitled to notice of the registration and have the right to include their shares in the registration. These registration rights are subject to specified conditions and limitations, including the right of the underwriters to limit the number of shares included in any such registration statement under certain circumstances.

Form S-3 Registration Rights

At any time after we are eligible to file a registration statement on Form S-3, upon the written request from the holders of at least 10% of the outstanding shares of registrable securities, holders of registrable securities have the right to demand that we file a registration statement on Form S-3 so long as the aggregate amount of shares to be offered and sold under such registration statement on Form S-3 is at least $1.0 million (net of any underwriters discounts or commissions). We are not required to effect a registration on Form S-3 if we have already effected two registrations on Form S-3 for the holders pursuant to Form S-3 Registration Rights within the twelve-month period preceding the date of the request. Additionally, we are not required to effect such registration in any jurisdiction in which we would be required to qualify to do business or execute a general consent of process in effecting such registration.

Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws

The provisions of Delaware law, our amended and restated certificate of incorporation and our amended and restated bylaws may have the effect of delaying, deferring or discouraging another person from acquiring control of our company. These provisions, which are summarized below, may have the effect of discouraging takeover bids. They are also designed, in part, to encourage persons seeking to acquire control of us to negotiate first with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate with an unfriendly or unsolicited acquirer outweigh the disadvantages of discouraging a proposal to acquire us because negotiation of these proposals could result in an improvement of their terms.

Delaware Law

We are governed by the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a public Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. A business combination includes mergers, asset sales or other transactions resulting in a financial benefit to the stockholder. An interested stockholder is a person who, together with affiliates and associates, owns, or within three years of the date on which it is sought to be determined whether such person is an interested stockholder, did own, 15% or more of the corporation s outstanding voting stock. These provisions may have the effect of delaying, deferring or preventing a change in our control.

Amended and Restated Certificate of Incorporation and Amended and Restated Bylaw Provisions

Our amended and restated certificate of incorporation and our amended and restated bylaws include a number of provisions that could deter hostile takeovers or delay or prevent changes in control of our management team, including the following:

Board of directors vacancies. Our amended and restated certificate of incorporation and amended and restated bylaws authorize only our board of directors to fill vacant directorships, including newly created seats. In addition, the number of directors constituting our board of directors is permitted to be

set only by a resolution adopted by our board of directors. These provisions prevent a stockholder from increasing the size of our board of directors and then gaining control of our board of directors by filling the resulting vacancies with its own nominees. This makes it more difficult to change the composition of our board of directors but promotes continuity of management.

Classified board. Our amended and restated certificate of incorporation and amended and restated bylaws provide that our board is classified into three classes of directors. A third party may be discouraged from making a tender offer or otherwise attempting to obtain control of us as it is more difficult and time consuming for stockholders to replace a majority of the directors on a classified board of directors. See Management Board Composition for additional information.

Stockholder action; special meeting of stockholders. Our amended and restated certificate of incorporation provides that our stockholders may not take action by written consent, but may only take action at annual or special meetings of our stockholders. As a result, a holder controlling a majority of our capital stock is not be able to amend our amended and restated bylaws or remove directors without holding a meeting of our stockholders called in accordance with our amended and restated bylaws. Our amended and restated bylaws further provide that special meetings of our stockholders may be called only by a majority of our board of directors, the Chairman of our Board of Directors, our Chief Executive Officer or our President, thus prohibiting a stockholder from calling a special meeting. These provisions might delay the ability of our stockholders to force consideration of a proposal or for stockholders controlling a majority of our capital stock to take any action, including the removal of directors.

Advance notice requirements for stockholder proposals and director nominations. Our amended and restated bylaws provide advance notice procedures for stockholders seeking to bring business before our annual meeting of stockholders or to nominate candidates for election as directors at our annual meeting of stockholders. Our amended and restated bylaws also specify certain requirements regarding the form and content of a stockholder s notice. These provisions might preclude our stockholders from bringing matters before our annual meeting of stockholders or from making nominations for directors at our annual meeting of stockholders if the proper procedures are not followed. We expect that these provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer s own slate of directors or otherwise attempting to obtain control of our company.

No cumulative voting. The Delaware General Corporation Law provides that stockholders are not entitled to the right to cumulate votes in the election of directors unless a corporation s certificate of incorporation provides otherwise. Our amended and restated certificate of incorporation does not provide for cumulative voting.

Directors removed only for cause. Our amended and restated certificate of incorporation provides that stockholders may remove directors only for cause.

Amendment of charter provisions. Any amendment of the above provisions in our amended and restated certificate of incorporation would require approval by holders of at least two-thirds of our then outstanding

voting securities.

Issuance of undesignated preferred stock. Our board of directors will have the authority, without further action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with rights and preferences, including voting rights, designated from time to time by our board of directors. The existence of authorized but unissued shares of preferred stock would enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or other means.

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Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Wells Fargo Bank, National Association. The transfer agent and registrar s address is Wells Fargo Bank, National Association, 110 Centre Pointe Curve, Suite 101, Mendota Heights, MN 55120-4101. Our shares of common stock are issued in uncertificated form only, subject to limited circumstances.

Market Listing

Our common stock is listed on The NASDAQ Global Select Market under the symbol OTIC.

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SHARES ELIGIBLE FOR FUTURE SALE

Future sales of our common stock in the public market, or the availability of such shares for sale in the public market, could adversely affect market prices prevailing from time to time. As described below, only a limited number of shares will be available for sale shortly after this offering due to contractual and legal restrictions on resale. Nevertheless, sales of our common stock in the public market after such restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price at such time and our ability to raise equity capital in the future.

Following the completion of this offering, based on the number of shares of our capital stock outstanding as of December 31, 2014, we will have a total of shares of our common stock outstanding, assuming no exercise of the underwriters option to purchase additional shares and no exercise of outstanding options and warrants. All of the shares of common stock sold in our initial public offering and sold in this offering, will be freely tradable without restriction or further registration under the Securities Act, unless these shares are held by our affiliates, as that term is defined in Rule 144 under the Securities Act, or are subject to the lock-up agreements described below.

The remaining outstanding shares of our common stock are restricted securities as defined in Rule 144. Restricted securities may be sold in the public market only if they are registered or if they qualify for an exemption from registration under Rule 144 or Rule 701 under the Securities Act, which rules are summarized below.

Subject to the provisions of Rule 144 or Rule 701, as applicable, and assuming no exercise of the underwriters option to purchase additional shares, of the shares of our common stock outstanding after this offering, the shares of our common stock will be available for sale in the public market as follows:

- are or will be immediately available for sale in the public market;
- 13,985,770 on February 9, 2015 upon the expiration of the lock-up agreements entered into in connection with our initial public offering; and
- 11,536,595 on the expiration of the lock-up agreements entered into in connection with this offering by each of our officers and directors, and certain of our securityholders.

Lock-Up Agreements

In connection with our initial public offering, we, our officers and directors and holders of substantially all of our common stock and securities convertible into or exchangeable for our common stock, agreed that, subject to certain exceptions and under certain conditions, for a period of 180 days after the date of the prospectus relating to our initial public offering, we and they will not, without the prior written consent of J.P. Morgan Securities LLC and Merrill Lynch, Pierce, Fenner & Smith Incorporated, dispose of or hedge any shares or any securities convertible into or exchangeable for shares of our capital stock. J.P. Morgan Securities LLC and Merrill Lynch, Pierce, Fenner & Smith Incorporated may, in their discretion, release any of the securities subject to these lock-up agreements at any time.

In the event that any holders of our common stock (including any securities convertible into or exercisable or exchangeable for common stock) are granted an early release, then the stockholders who are party to our amended and restated stockholders agreement will be granted an early release from their obligations under the lock-up agreement on

a pro rata basis.

Beginning on February 9, 2015, subject to the lock-up agreements entered into in connection with this offering discussed below, the shares subject to the lock-up agreements described above may be sold in the public market in the United States, subject to prior registration in the United States, if required, or reliance upon an exemption from registration, including, in the case of shares held by affiliates or control persons, compliance with the volume restrictions of Rule 144.

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Additionally, in connection with this offering, we, along with each of our officers and directors, and certain of our securityholders, have agreed with the underwriters of this offering, subject to certain exceptions, not to dispose of or hedge any of their common stock or securities convertible into or exchangeable or exercisable for shares of common stock for a period of 90 days after the date of this prospectus, except with the prior written consent of J.P. Morgan Securities LLC.

Rule 144

In general, under Rule 144 as currently in effect, a person who is not deemed to have been one of our affiliates for purposes of the Securities Act at any time during the 90 days preceding a sale and who has beneficially owned the shares proposed to be sold for at least six months, including the holding period of any prior owner other than our affiliates, is entitled to sell those shares without complying with the manner of sale, volume limitation or notice provisions of Rule 144, subject to compliance with the public information requirements of Rule 144. If such a person has beneficially owned the shares proposed to be sold for at least one year, including the holding period of any prior owner other than our affiliates, then that person would be entitled to sell those shares without complying with any of the requirements of Rule 144.

In general, under Rule 144, as currently in effect, and upon expiration of the lock-up agreements described above, our affiliates or persons selling shares on behalf of our affiliates are entitled to sell within any three-month period, a number of shares that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately shares immediately after this offering assuming no exercise by the underwriters of their option to purchase additional shares of common stock from us in this offering; or
- the average weekly trading volume of our common stock during the four calendar weeks preceding the filing of a notice on Form 144 with respect to that sale.

Sales under Rule 144 by our affiliates or persons selling shares on behalf of our affiliates are also subject to certain manner of sale provisions and notice requirements and to the availability of current public information about us. Rule 144 also provides that affiliates relying on Rule 144 to sell shares of our common stock that are not restricted shares must nonetheless comply with the same restrictions applicable to restricted shares, other than the holding period requirement.

Notwithstanding the availability of Rule 144, our officers and directors have entered into lock-up agreements as described above and their restricted shares will become eligible for sale at the expiration of the restrictions set forth in those agreements.

Rule 701

Rule 701 generally allows a stockholder who purchased shares of our common stock pursuant to a written compensatory plan or contract and who is not deemed to have been an affiliate of our company during the immediately preceding 90 days to sell these shares in reliance upon Rule 144, but without being required to comply with the public information, holding period, volume limitation or notice provisions of Rule 144. Rule 701 also permits affiliates of our company to sell their Rule 701 shares under Rule 144 without complying with the holding period requirements of Rule 144.

Registration Rights

The holders of an aggregate of up to 14,079,588 shares of our common stock, including shares of common stock issuable upon the exercise of outstanding options and warrants, or their permitted transferees, are entitled to various rights with respect to the registration of these shares under the Securities Act, subject to the lock-up agreements described above. Registration of these shares under the Securities Act would result in these

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shares becoming fully tradable without restriction under the Securities Act immediately upon the effectiveness of the registration, except for shares purchased by affiliates. See the section titled Description of Capital Stock Registration Rights for additional information.

Equity Incentive Plans

We filed a registration statement on Form S-8 under the Securities Act to register shares of our common stock subject to outstanding stock options and all shares reserved for issuance under our equity compensation plans. Shares covered by such registration statement are eligible for sale in the public market, subject to vesting restrictions, the lock-up agreements described above and Rule 144 limitations applicable to affiliates. See the section titled Executive Compensation Employee Benefit and Stock Plans for additional information.

Warrants

As of December 31, 2014, warrants entitling holders to purchase an aggregate of 142,113 shares of our common stock at an exercise price of $14.1765 per share were outstanding.

See the section titled Description of Capital Stock for additional information. Such shares issued upon exercise of the warrants may be able to be sold after the expiration of the lock-up periods described above subject the requirements of Rule 144 described above.

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MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following is a summary of the material U.S. federal income tax consequences of the ownership and disposition of our common stock to non-U.S. holders (as defined below), but does not purport to be a complete analysis of all the potential tax considerations relating thereto. This summary is based upon the provisions of the United States Internal Revenue Code of 1986, as amended, or the Code, Treasury Regulations promulgated thereunder, administrative rulings and judicial decisions, all as of the date hereof. These authorities may be changed, possibly retroactively, so as to result in U.S. federal income tax consequences different from those set forth below. We have not sought any ruling from the Internal Revenue Service (IRS) with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions.

This summary also does not address the tax considerations arising under the laws of any non-U.S., state or local jurisdiction or under U.S. federal gift and estate tax laws, except to the limited extent set forth below. In addition, this discussion does not address any tax considerations applicable to an investor s particular circumstances or to investors that may be subject to special tax rules, including, without limitation:

banks, insurance companies or other financial institutions;

persons subject to the alternative minimum tax or the tax on net investment income;

tax-exempt organizations;

controlled foreign corporations, passive foreign investment companies and corporations that accumulate earnings to avoid U.S. federal income tax;

dealers in securities or currencies;

traders in securities that elect to use a mark-to-market method of accounting for their securities holdings;

persons that own, or are deemed to own, more than five percent of our capital stock (except to the extent specifically set forth below);

certain former citizens or long-term residents of the United States;

persons who hold our common stock as a position in a hedging transaction, straddle, conversion transaction or other risk reduction transaction;

persons who hold or receive our common stock pursuant to the exercise of any warrant or option or otherwise as compensation;

persons who do not hold our common stock as a capital asset within the meaning of Section 1221 of the Code; or

persons deemed to sell our common stock under the constructive sale provisions of the Code.

In addition, if a partnership, or entity or arrangement classified as a partnership for U.S. federal income tax purposes, holds our common stock, the tax treatment of a partner generally will depend on the status of the partner and upon the activities of the partnership. Accordingly, partnerships that hold our common stock, and partners in such partnerships, should consult their tax advisors.

You are urged to consult your tax advisor with respect to the application of the U.S. federal income tax laws to your particular situation, as well as any tax consequences of the purchase, ownership and disposition of our common stock arising under the U.S. federal estate or gift tax laws or under the laws of any state, local, non-U.S. or other taxing jurisdiction or under any applicable tax treaty.

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Non-U.S. Holder Defined

For purposes of this discussion, you are a non-U.S. holder if you are any holder other than a partnership (or other entity classified as a partnership for U.S. federal income tax purposes), or a partner in a partnership, or:

an individual citizen or resident of the United States (for U.S. federal income tax purposes);

a corporation or other entity taxable as a corporation created or organized in the United States or under the laws of the United States or any political subdivision thereof;

an estate whose income is subject to U.S. federal income tax regardless of its source; or

a trust (x) whose administration is subject to the primary supervision of a U.S. court and that has one or more U.S. persons who have the authority to control all substantial decisions of the trust or (y) that has made a valid election under applicable Treasury Regulations to be treated as a U.S. person.

Distributions

We do not anticipate making any distributions on our common stock following the completion of this offering. However, if we do make distributions on our common stock, those payments will constitute dividends for U.S. tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed both our current and our accumulated earnings and profits, they will constitute a return of capital and will first reduce your basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock.

Subject to the discussion below on effectively connected income and foreign accounts, any dividend paid to you generally will be subject to U.S. withholding tax either at a rate of 30% of the gross amount of the dividend or such lower rate as may be specified by an applicable income tax treaty. In order to receive a reduced treaty rate, you must provide us with an IRS Form W-8BEN or W-8BEN-E or other appropriate version of IRS Form W-8 certifying qualification for the reduced rate. A non-U.S. holder of shares of our common stock eligible for a reduced rate of U.S. withholding tax pursuant to an income tax treaty may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. If the non-U.S. holder holds the stock through a financial institution or other agent acting on the non-U.S. holder s behalf, the non-U.S. holder will be required to provide appropriate documentation to the agent, which then will be required to provide certification to us or our paying agent, either directly or through other intermediaries.

Dividends received by you that are effectively connected with your conduct of a U.S. trade or business (and, if required by an applicable income tax treaty, such dividends are attributable to a permanent establishment maintained by you in the United States), are includible in your gross income in the taxable year received, and are generally exempt from such withholding tax, subject to the discussion below on backup withholding and foreign accounts. In order to obtain this exemption, you must provide us with an IRS Form W-8ECI or other applicable IRS Form W-8 properly certifying such exemption. Such effectively connected dividends, although not subject to withholding tax, are taxed at the same graduated rates applicable to U.S. persons, net of certain deductions and credits, subject to an applicable income tax treaty providing otherwise. In addition, if you are a corporate non-U.S. holder, dividends you

receive that are effectively connected with your conduct of a U.S. trade or business may also be subject to a branch profits tax at a rate of 30% or such lower rate as may be specified by an applicable income tax treaty. You should consult your tax advisor regarding any applicable tax treaties that may provide for different rules.

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Gain on Disposition of Common Stock

Subject to the discussion below on backup withholding and foreign accounts, you generally will not be required to pay U.S. federal income tax on any gain realized upon the sale or other disposition of our common stock unless:

- the gain is effectively connected with your conduct of a U.S. trade or business (and, if required by an applicable income tax treaty, the gain is attributable to a permanent establishment maintained by you in the United States);
- you are an individual who is present in the United States for a period or periods aggregating 183 days or more during the calendar year in which the sale or disposition occurs and certain other conditions are met; or
- our common stock constitutes a U.S. real property interest by reason of our status as a United States real property holding corporation, or USRPHC, for U.S. federal income tax purposes at any time within the shorter of the five-year period preceding your disposition of, or your holding period for, our common stock.

We believe that we are not currently and will not become a USRPHC. However, because the determination of whether we are a USRPHC depends on the fair market value of our U.S. real property relative to the fair market value of our other business assets, there can be no assurance that we will not become a USRPHC in the future. Even if we become a USRPHC, however, as long as our common stock is regularly traded on an established securities market, your common stock will be treated as U.S. real property interests only if you actually or constructively hold more than five percent of such regularly traded common stock at any time during the shorter of the five-year period preceding your disposition of, or your holding period for, our common stock.

If you are a non-U.S. holder described in the first bullet above, you will be required to pay tax on the net gain derived from the sale under regular graduated U.S. federal income tax rates, and a corporate non-U.S. holder described in the first bullet above also may be subject to the branch profits tax at a 30% rate, or such lower rate as may be specified by an applicable income tax treaty. If you are an individual non-U.S. holder described in the second bullet above, you will be subject to tax at 30% (or such lower rate specified by an applicable income tax treaty) on the gain derived from the sale, which tax may be offset by U.S. source capital losses for the year. You should consult any applicable income tax or other treaties that may provide for different rules.

Federal Estate Tax

Our common stock beneficially owned by an individual who is not a citizen or resident of the United States (as defined for U.S. federal estate tax purposes) at the time of their death will generally be includable in the decedent s gross estate for U.S. federal estate tax purposes, unless an applicable estate tax treaty provides otherwise.

Backup Withholding and Information Reporting

Generally, we must report annually to the IRS the amount of dividends paid to you, your name and address, and the amount of tax withheld, if any. A similar report will be sent to you. Pursuant to applicable income tax treaties or other agreements, the IRS may make these reports available to tax authorities in your country of residence.

Payments of dividends or of proceeds on the disposition of stock made to you may be subject to information reporting and backup withholding at a current rate of 28% unless you establish an exemption, for example, by properly certifying your non-U.S. status on an IRS Form W-8BEN or W-8BEN-E or another appropriate version of IRS Form W-8. Notwithstanding the foregoing, backup withholding and information reporting may apply if either we or our paying agent has actual knowledge, or reason to know, that you are a U.S. person.

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Backup withholding is not an additional tax; rather, the U.S. federal income tax liability of persons subject to backup withholding will be reduced by the amount of tax withheld. If withholding results in an overpayment of taxes, a refund or credit may generally be obtained from the IRS, provided that the required information is furnished to the IRS in a timely manner.

Foreign Accounts

Code Sections 1471-1474 and the regulations issued thereunder generally impose a U.S. federal withholding tax of 30% on dividends on, and the gross proceeds from a sale or other disposition of our common stock, paid to a foreign financial institution (as specially defined under these rules), unless such institution enters into an agreement with the U.S. government to, among other things, withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding the U.S. account holders of such institution (which includes certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with U.S. owners) or otherwise establishes an exemption. The provisions also generally impose a U.S. federal withholding tax of 30% on dividends on and the gross proceeds from a sale or other disposition of our common stock paid to a non-financial foreign entity (as defined under these rules) unless such entity provides the withholding agent with a certification identifying the direct and indirect U.S. owners of the entity or otherwise establishes an exemption. The withholding obligations under these provisions generally apply to dividends on our common stock and, under current transitional rules, are expected to apply with respect to the gross proceeds of a sale or other disposition of our common stock on or after January 1, 2017. Under certain circumstances, a non-U.S. holder might be eligible for refunds or credits of such taxes. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this paragraph. Prospective investors are encouraged to consult with their own tax advisors regarding the possible implications of this legislation on their investment in our common stock.

The preceding discussion of U.S. federal tax considerations is for general information only. It is not tax advice. Each prospective investor should consult its own tax advisor regarding the particular U.S. federal, state and local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed change in applicable laws.

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UNDERWRITING

We are offering the shares of common stock described in this prospectus through a number of underwriters. J.P. Morgan Securities LLC is acting as sole book-running manager of the offering and as representative of the underwriters. We will enter into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we will agree to sell to the underwriters, and each underwriter will severally agree to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus, the number of shares of common stock listed next to its name in the following table:

Underwriters	Number of Shares
J.P. Morgan Securities LLC	
Piper Jaffray & Co	
Cowen and Company, LLC	
Sanford C. Bernstein & Co., LLC	
Total	

The underwriters will be committed to purchase all the common shares offered by us if they purchase any shares. The underwriting agreement will also provide that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the common shares directly to the public at the public offering price set forth on the cover page of this prospectus and to certain dealers at that price less a concession not in excess of $ per share. Sales of shares made outside of the United States may be made by affiliates of the underwriters.

The underwriters will have an option to buy up to additional shares of common stock from us. The underwriters will have 30 days from the date of this prospectus to exercise this option. If any shares are purchased with this option, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is $ per share. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters option to purchase additional shares.

	Without Exercise of Option to Purchase Additional Shares	With Full Exercise of Option to Purchase Additional Shares
Per Share	$	$
Total	$	$

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately $ million. We have agreed to reimburse the underwriters for all expenses relating to the clearance of this offering with the Financial Industry Regulatory Authority in an amount not to exceed $25,000.

A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to

allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representative to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We have agreed that we will not (i) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise dispose of, directly or indirectly, or file with the SEC a registration statement under the Securities Act relating to, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (ii) enter into any swap or other arrangement that transfers all or a portion of the economic consequences associated with the ownership of any shares of common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of common stock or such other securities, in cash or otherwise), in each case without the prior written consent of J.P. Morgan Securities LLC for a period of 90 days after the date of this prospectus. Subject to certain conditions, these restrictions will not apply to (i) shares of our common stock to be sold in this offering, (ii) any shares of our common stock issued upon the exercise of options granted under our existing equity incentive plans or warrants described as outstanding in the registration statement of which this prospectus forms a part, provided that we shall use commercially reasonable efforts to cause the recipient of such shares of our common stock issued pursuant to this clause (ii) during the 90-day restricted period described above to enter into a lock-up agreement, (iii) any options and other awards granted under an equity incentive plan described in the registration statement of which this prospectus forms a part, (iv) the filing of any registration statement on Form S-8 or a successor form thereto relating to an equity incentive plan described in the registration statement of which this prospectus forms a part, and (v) shares of our common stock or other securities issued in connection with a transaction with an unaffiliated third party that includes a bona fide commercial relationship (including joint ventures, marketing or distribution arrangements, collaboration agreements or intellectual property license agreements) or any acquisition of assets or acquisition of not less than a majority or controlling portion of the equity of another entity, provided that (x) the aggregate number of shares issued pursuant to this clause (v) shall not exceed five percent (5%) of the total number of outstanding shares of common stock immediately following the issuance and sale of the shares of common stock in this offering and (y) the recipient of any such shares of common stock and securities issued pursuant to this clause (v) during the 90-day restricted period described above shall enter into a lock-up agreement.

Our directors, executive officers and certain of our securityholders have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons or entities, with limited exceptions, for a period of 90 days after the date of this prospectus, may not, without the prior written consent of J.P. Morgan Securities LLC, (1) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such directors, executive officers, managers and members in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant) or (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or such other securities, in cash or otherwise, or (3) make any demand for or exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock. The restrictions described in the immediately preceding paragraph do not apply to certain transactions, including:

shares to be purchased or sold pursuant to the underwriting agreement in this offering;

common stock acquired in open market transactions on or after the date of this prospectus, provided that no filing by any party (donor, donee, transferor or transferee) under the Exchange Act or other

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public announcement shall be required or shall be made voluntarily in connection with such transfer or distribution (other than a filing on a Form 5 made after the expiration of the lock-up period);

transfers of common stock (i) as a bona fide gift, (ii) to any trust for the direct or indirect benefit of the undersigned or the immediately family member of the undersigned, or if the undersigned is a trust, to any beneficiary (including such beneficiary s estate) of the undersigned, (iii) by will or intestate succession upon the death of the undersigned, or (iv) to another corporation, partnership, limited liability company, trust or other business entity that is a direct or indirect affiliate (as defined in Rule 405 promulgated under the Securities Act) of the party subject to the lock-up restrictions or as part of a distribution without consideration to stockholders, beneficiaries, partners, members or other equity holders, provided that in the case of any transfer contemplated in clauses (i) through (iv) above, each donee, heir, distributee or other transferee shall execute and deliver a lock-up letter substantially in the form executed by the party subject to the lock-up restrictions, and provided, further, that no filing by any party (donor, donee, transferor or transferee) under the Exchange Act or other public announcement shall be required or shall be made voluntarily in connection with such transfer or distribution (other than a filing on a Form 5 made after the expiration of the lock-up period);

the net or cashless exercise of options to purchase common stock or settlement of restricted stock units pursuant to our equity incentive plans or of warrants to purchase our securities, or the exchange or conversion of any securities convertible or exchangeable for common stock granted pursuant to our equity incentive plans, in each case which equity incentive plans and warrants are described in this prospectus, provided that any exercise or settlement does not involve a sale of securities to any person or entity other than us, whether to cover the applicable exercise price, withholding tax obligation or otherwise, provided, further, that the securities received upon such exercise, settlement, exchange or conversion shall be subject to the terms of this letter agreement and that no filing by any party under the Exchange Act or other public announcement shall be required or shall be made voluntarily in connection therewith (other than a filing on a Form 5 made after the expiration of the lock-up period);

dispositions to us pursuant to agreements under which the shares were issued and we have the option to repurchase such shares or securities or a right of first refusal with respect to transfers of such shares or securities, provided that no filing under Section 16(a) of the Exchange Act shall be required or shall be voluntarily made within 30 days after the date of this prospectus, and after such 30th day, any filing under Section 16(a) of the Exchange Act shall clearly indicate in the footnotes thereto that (i) the filing relates to the transfer of such shares or securities to the Company pursuant to such repurchase option or right of first refusal, as the case may be, and (ii) no shares were sold by the reporting person;

in connection with the conversion of our outstanding preferred stock into shares of our common stock, provided that the securities so received shall be subject to the restrictions on transfer set forth in the agreement;

pursuant to a bona fide third-party tender offer, merger, consolidation or other similar transaction made to all holders of our capital stock involving a change of control of the Company, provided that in the event that such tender offer, merger, consolidation or other such transaction is not completed, the securities held by the

party subject to the lock-up restrictions shall remain subject to such restrictions;

transfers by operation of law, such as pursuant to a domestic relations order or in connection with a divorce settlement, provided that any transferee shall execute and deliver a lock-up letter substantially in the form executed by the party subject to the lock-up restrictions; or

the establishment of a written plan meeting the requirements of Rule 10b5-1 under the Exchange Act relating to the sale of securities, provided that the securities subject to such plan may not be sold and no public disclosure of any such action shall be required or shall be voluntarily made by any person during the lock-up period.

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We will agree to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act.

Our common stock is listed on The NASDAQ Global Select Market under the symbol OTIC.

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of the common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be covered shorts, which are short positions in an amount not greater than the underwriters option to purchase additional shares referred to above, or may be naked shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through their option. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representative of the underwriters purchases common stock in the open market in stabilizing transactions or to cover short sales, the representative can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on NASDAQ, in the over-the-counter market or otherwise.

Neither we nor the underwriters can assure investors that an active trading market will develop for our common shares, or that the shares will trade in the public market at or above the public offering price.

Selling Restrictions

General

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

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United Kingdom

Each underwriter has represented and agreed that:

(1) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the FSMA) received by it in connection with the issue or sale of our common shares in circumstances in which Section 21(1) of the FSMA does not apply to us; and

(2) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to our common shares in, from or otherwise involving the United Kingdom.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), an offer to the public of any shares which are the subject of the offering contemplated by this prospectus (the Shares) may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of any Shares may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

(1) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

(2) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representative for any such offer; or

(3) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of Shares shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an offer to the public in relation to any Shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any Shares to be offered so as to enable an investor to decide to purchase any Shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State, and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or the SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made

publicly available in Switzerland.

Neither this prospectus nor any other offering or marketing material relating to the offering, the Company, the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this

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document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or the CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Hong Kong

The shares may not be offered or sold by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), or (ii) to professional investors within the meaning of the Securities and Futures Ordinance (Cap.571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a prospectus within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the SFA), (ii) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 by a relevant person which is: (a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries rights and interest in that trust shall not be transferable for 6 months after that corporation or that trust has acquired the shares under Section 275 except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA; (2) where no consideration is given for the transfer; or (3) by operation of law.

Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (the Financial Instruments and Exchange Law) and each underwriter has agreed that it will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and

Exchange Law and any other applicable laws, regulations and ministerial guidelines of Japan.

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Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future.

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LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California. The underwriters are being represented by Cooley LLP, San Diego, California, in connection with this offering. Certain members of, and investment partnerships comprised of members of, and persons associated with, Wilson Sonsini Goodrich & Rosati, Professional Corporation, own an aggregate of 16,215 shares of our common stock and warrants to purchase 1,053 shares of our common stock.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements as of December 31, 2013 and 2012, and for the years then ended, as set forth in their report. We have included our financial statements in the prospectus and elsewhere in the registration statement in reliance on Ernst & Young LLP s report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock offered by this prospectus. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement, some of which is contained in exhibits to the registration statement as permitted by the rules and regulations of the SEC. For further information with respect to us and our common stock, we refer you to the registration statement, including the exhibits filed as a part of the registration statement. Statements contained in this prospectus concerning the contents of any contract or any other document is not necessarily complete. If a contract or document has been filed as an exhibit to the registration statement, please see the copy of the contract or document that has been filed. Each statement in this prospectus relating to a contract or document filed as an exhibit is qualified in all respects by the filed exhibit. You may obtain copies of this information by mail from the Public Reference Section of the SEC, 100 F Street, N.E., Room 1580, Washington, D.C. 20549, at prescribed rates. You may obtain information on the operation of the public reference rooms by calling the SEC at 1-800-SEC-0330. The SEC also maintains an Internet website that contains reports, proxy statements and other information about issuers, like us, that file electronically with the SEC. The address of that website is www.sec.gov.

We are subject to the information and reporting requirements of the Exchange Act and, in accordance with this law, are required to file periodic reports, proxy statements and other information with the SEC. These periodic reports, proxy statements and other information are available for inspection and copying at the SEC s public reference facilities and the website of the SEC referred to above. We also maintain a website at www.otonomy.com. You may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. Information contained on our website is not a part of this prospectus and the inclusion of our website address in this prospectus is an inactive textual reference only.

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Otonomy, Inc.

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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, 2012 and 2013, and the related statements of operations, convertible preferred stock and stockholders deficit and cash flows for the years then ended. 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, 2012 and 2013, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

San Diego, California

June 5, 2014,

except for the retrospective adoption of amendments to the accounting standards relating to the financial reporting distinction between development stage entities and other reporting entities as described in Note 1, as to which the date is

July 28, 2014,

and except for the reverse stock split described in paragraph 10 of Note 11, as to which the date is

July 31, 2014

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Otonomy, Inc.

Balance Sheets

(in thousands, except share and per share data)

	December 31, 2012	2013	September 30, 2014 (unaudited)
Assets			
Current assets:			
Cash	$ 4,663	$ 37,284	$ 165,155
Restricted cash	50	75	
Prepaid and other current assets	697	1,654	2,177
Total current assets	5,410	39,013	167,332
Property and equipment, net	439	683	952
Other long-term assets	55	61	41
Total assets	$ 5,904	$ 39,757	$ 168,325
Liabilities, Convertible Preferred Stock and Stockholders (Deficit) Equity			
Current liabilities:			
Accounts payable	$ 1,134	$ 2,014	$ 1,748
Accrued expenses	315	384	2,486
Accrued compensation	184	244	1,254
Current portion of deferred rent	51	73	83
Total current liabilities	1,684	2,715	5,571
Convertible preferred stock warrant liability	2,909	646	
Convertible notes payable and accrued interest, net of debt discount	7,065		
Deferred rent, net of current portion	266	220	156
Total liabilities	11,924	3,581	5,727
Commitments and Contingencies			
Convertible preferred stock, $0.001 par value; 3,575,085 shares authorized at December 31, 2012; 9,519,809 shares authorized at December 31, 2013 and no shares authorized at September 30, 2014 (unaudited)			
Series A convertible preferred stock, 406,712 shares designated at December 31, 2012; 404,671 shares designated at December 31, 2013 and no shares designated at September 30, 2014 (unaudited); $2,987 liquidation preference at December 31, 2013; no shares issued or outstanding at September 30, 2014 (unaudited)	10,559	10,561	

Series B convertible preferred stock, 3,168,373 shares designated at December 31, 2012; 1,708,076 shares designated at December 31, 2013 and no shares designated at September 30, 2014 (unaudited); $15,014 liquidation preference at December 31, 2013; no shares issued or outstanding at September 30, 2014 (unaudited)	22,488	23,007
Series C convertible preferred stock, no shares designated at December 31, 2012; 7,407,062 shares designated at December 31, 2013 and no shares designated at September 30, 2014 (unaudited); $92,823 liquidation preference at December 31, 2013; no shares issued or outstanding at September 30, 2014 (unaudited)		61,585

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Otonomy, Inc.,

Balance Sheets (Continued)

(in thousands, except share and per share data)

	December 31, 2012	2013	September 30, 2014 (unaudited)
Stockholders (deficit) equity:			
Preferred stock, $0.001 par value, no shares authorized at December 31, 2012 and December 31, 2013; 10,000,000 shares authorized at September 30, 2014 (unaudited); no shares issued or outstanding at December 31, 2012, December 31, 2013 and September 30, 2014 (unaudited)	$	$	$
Common stock, $0.001 par value; 4,707,053 shares authorized at December 31, 2012; 11,851,717 shares authorized at December 31, 2013 and 200,000,000 shares authorized at September 30, 2014 (unaudited); 73,697 shares issued and outstanding at December 31, 2012; 75,325 shares issued and outstanding as of December 31, 2013 and 21,172,221 shares issued and outstanding at September 30, 2014 (unaudited)			21
Additional paid-in capital	392	580	255,252
Accumulated deficit	(39,459)	(59,557)	(92,675)
Total stockholders (deficit) equity	(39,067)	(58,977)	162,598
Total liabilities, convertible preferred stock, and stockholders (deficit) equity	$ 5,904	$ 39,757	$ 168,325

See accompanying notes.

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Otonomy, Inc.

Statements of Operations

(in thousands, except share and per share data)

	Years Ended December 31,		Nine Months Ended September 30,	
	2012	2013	2013	2014
			(unaudited)	
Operating expenses:				
Research and development	$ 8,523	$ 16,336	$ 9,698	$ 24,616
General and administrative	2,408	3,514	2,284	5,169
Total operating expenses	10,931	19,850	11,982	29,785
Loss from operations	(10,931)	(19,850)	(11,982)	(29,785)
Other income (expense):				
Interest expense	(444)	(2,528)	(2,524)	(39)
Change in fair value of convertible preferred stock warrant liability	100	2,833	2,713	(3,300)
Change in fair value of convertible preferred stock purchase right	3,707			
Other (expense) income, net	(1)	(14)	(9)	41
Total other income (expense)	3,362	291	180	(3,298)
Net loss and comprehensive loss	(7,569)	(19,559)	(11,802)	(33,083)
Accretion to redemption value of convertible preferred stock	(801)	(539)	(526)	(35)
Net loss attributable to common stockholders	$ (8,370)	$ (20,098)	$ (12,328)	$ (33,118)
Net loss per share attributable to common stockholders, basic and diluted	$ (118.99)	$ (268.79)	$ (165.29)	$ (9.83)
Weighted-average shares used to compute net loss per share attributable to common stockholders, basic and diluted	70,343	74,772	74,585	3,369,437

See accompanying notes.

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Otonomy, Inc.

Statements of Convertible Preferred Stock and Stockholders (Deficit) Equity

(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	Accu
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			
								60,925	98	
								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

See accompanying notes.

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Otonomy, Inc.

Statements of Convertible Preferred Stock and Stockholders (Deficit) Equity (Continued)

(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 Capital	Accumulated Deficit	Total Stockholders (Deficit) Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount			
Reclassification of convertible preferred stock warrant liability to additional paid-in capital (unaudited)	$		$		$		$			$	$ 3,946	$	$ 3,946
Stock-based compensation expense (unaudited)											895		895
Accretion to redemption value of convertible preferred stock (unaudited)						31		4				(35)	(35)
Net loss (unaudited)												(33,083)	(33,083)
Balance at September 30, 2014 (unaudited)	$		$		$		$		21,172,221	$ 21	$ 255,252	$ (92,675)	$ 162,598

See accompanying notes.

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Otonomy, Inc.,

Statements of Cash Flows

(in thousands)

	Years Ended December 31,		Nine Months Ended September 30,	
	2012	2013	2013	2014
			(unaudited)	
Cash flows from operating activities:				
Net loss	$ (7,569)	$ (19,559)	$ (11,802)	$ (33,083)
Adjustments to reconcile net loss to net cash used in operating activities:				
Depreciation and amortization	192	257	194	152
Stock-based compensation	191	183	125	895
Non-cash interest expense	444	2,528	2,524	39
Change in fair value of convertible preferred stock warrant liability	(100)	(2,833)	(2,713)	3,300
Change in fair value of convertible preferred stock purchase right	(3,707)			
Deferred rent	317	(24)	(9)	(54)
Changes in operating assets and liabilities:				
Prepaid and other assets	(530)	(1,013)	(74)	(542)
Accounts payable	641	874	(249)	(814)
Accrued expenses	(472)	60	450	2,076
Accrued compensation	(235)	60	413	1,010
Net cash used in operating activities	(10,828)	(19,467)	(11,141)	(27,021)
Cash flows from investing activities:				
(Increase) decrease in restricted cash		(25)		75
Purchases of property and equipment	(185)	(486)	(445)	(402)
Net cash used in investing activities	(185)	(511)	(445)	(327)
Cash flows from financing activities:				
Proceeds from convertible notes payable	8,011	7,009	7,009	
Proceeds from issuance of convertible preferred stock, net of issuance costs		45,585	22,641	49,239
Proceeds from issuance of common stock in initial public offering, net of fees				104,681
Proceeds from issuance of restricted common stock and exercise of stock options, net of early exercise liability	3	5	5	98
Proceeds from exercise of preferred stock warrants				1,201

Net cash provided by financing activities	8,014	52,599	29,655	155,219
Net change in cash	(2,999)	32,621	18,069	127,871
Cash at beginning of period	7,662	4,663	4,663	37,284
Cash at end of period	$ 4,663	$ 37,284	$ 22,732	$ 165,155
Supplemental disclosure of non-cash investing and financing activities:				
Purchase of property and equipment in accounts payable and accrued expenses	$	$ 15	$ 7	$ 19
Conversion of convertible notes payable and accrued interest into convertible preferred stock	$	$ 15,982	$ 15,982	$
Initial public offering costs in accounts payable and accrued expenses	$	$	$	$ 555

See accompanying notes.

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Otonomy, Inc.,

Notes to Financial Statements

(information as of September 30, 2014 and for the nine months ended

September 30, 2013 and 2014 is unaudited)

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. 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 approximately $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.

Basis of Presentation

As of December 31, 2013 and September 30, 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, 2013, the Company had working capital of $36.3 million and an accumulated deficit of $59.6 million. As of September 30, 2014, the Company had working capital of $161.8 million and an accumulated deficit of $92.7 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 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.

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Otonomy, Inc.,

Notes to Financial Statements (Continued)

(information as of September 30, 2014 and for the nine months ended

September 30, 2013 and 2014 is unaudited)

Recently Issued Accounting Standards

In June 2014, new guidance was issued 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 statements of operations, stockholders (deficit) equity and cash flows or 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 standards are to be applied retrospectively and impact the presentation of the financial statements, but do not impact the Company s financial position or results of operations.

Unaudited Interim Financial Information

The accompanying interim balance sheet as of September 30, 2014, statements of operations, and cash flows for the nine months ended September 30, 2013 and 2014, the statements of convertible preferred stock and stockholders (deficit) equity for the nine months ended September 30, 2014 and the related footnote disclosures are unaudited. These unaudited interim financial statements have been prepared on the same basis as the annual audited financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments necessary for the fair statement of the Company s financial position as of September 30, 2014, and the results of its operations and cash flows for the nine months ended September 30, 2013 and 2014. The results for the nine months ended September 30, 2014 are not necessarily indicative of results to be expected for the year ending December 31, 2014, or any other interim or future year or period.

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, clinical trial accruals and the valuation of convertible preferred stock warrants. 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. Deposits in the Company s checking account are maintained in federally insured

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Otonomy, Inc.,

Notes to Financial Statements (Continued)

(information as of September 30, 2014 and for the nine months ended

September 30, 2013 and 2014 is unaudited)

financial institutions in excess of federally insured limits. The Company has not experienced any losses in such accounts and believes it is not exposed to significant risk on its cash balances due to the financial position of the depository institution in which those deposits are held. Additionally, the Company established guidelines regarding approved investments and maturities of investments, which are designed to maintain safety and liquidity.

Cash

Cash consists of cash and highly liquid investments with original maturities of three months or less at the date of purchase. Cash is readily available in checking and savings accounts.

Restricted Cash

Restricted cash is comprised of cash held by a bank to securitize the Company s corporate credit card.

Fair Value of Financial Instruments

The carrying value of the Company s cash, restricted cash, 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. The convertible preferred stock warrant liability is carried at fair value (see Note 6).

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 September 30, 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.

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Otonomy, Inc.,

Notes to Financial Statements (Continued)

(information as of September 30, 2014 and for the nine months ended

September 30, 2013 and 2014 is unaudited)

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, 2012 and 2013, and the nine months ended September 30, 2014, 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.

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

Otonomy, Inc.,

Notes to Financial Statements (Continued)

(information as of September 30, 2014 and for the nine months ended

September 30, 2013 and 2014 is unaudited)

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 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 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

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Otonomy, Inc.,

Notes to Financial Statements (Continued)

(information as of September 30, 2014 and for the nine months ended

September 30, 2013 and 2014 is unaudited)

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.

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,		As of September 30,	
	2012	2013	2013	2014
			(unaudited)	
Convertible preferred stock	2,453,463	9,493,489	6,882,572	

Convertible notes payable	580,580			
Warrants to purchase convertible preferred stock	255,013	483,517	483,517	
Warrants to purchase common stock				142,113
Unvested restricted common stock subject to repurchase	859			16,294
Options to purchase common stock	382,663	1,235,705	373,375	2,058,910
	3,672,578	11,212,711	7,739,464	2,217,317

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Otonomy, Inc.,

Notes to Financial Statements (Continued)

(information as of September 30, 2014 and for the nine months ended

September 30, 2013 and 2014 is unaudited)

3. Balance Sheet Details

Prepaid and Other Current Assets

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

	December 31, 2012	2013	September 30, 2014 (unaudited)
Prepaid clinical trial costs	$ 500	$ 1,478	$ 1,054
Other	197	176	1,123
Total	$ 697	$ 1,654	$ 2,177

Property and Equipment, Net

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

	December 31, 2012	2013	September 30, 2014 (unaudited)
Laboratory equipment	$ 827	$ 908	$ 1,088
Manufacturing equipment		392	607
Computer equipment and software	102	93	114
Leasehold improvements	138	67	67
Office furniture	15	17	17
	1,082	1,477	1,893
Less: accumulated depreciation and amortization	(643)	(794)	(941)
Total	$ 439	$ 683	$ 952

Depreciation expense was $0.2 million and $0.3 million for the years ended December 31, 2012 and 2013, respectively. Depreciation expense was $0.2 million for each of the nine month periods ended September 30, 2013

and 2014.

Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31,		September 30,
	2012	2013	2014
			(unaudited)
Accrued clinical trial costs	$ 197	$ 196	$ 1,892
Accrued other	118	188	594
Total	$ 315	$ 384	$ 2,486

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Otonomy, Inc.,

Notes to Financial Statements (Continued)

(information as of September 30, 2014 and for the nine months ended

September 30, 2013 and 2014 is unaudited)

4. Notes Payable and Convertible Preferred Stock Warrants

2012 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). The 2012 Notes had an interest rate of 8% per annum and were secured by all of the Company s assets. The 2012 Notes were convertible into shares of the Company s equity securities sold at the next financing yielding gross proceeds to the Company of at least $10.0 million.

In connection with the issuance of the 2012 Notes, the Company issued warrants for the purchase of 182,082 shares of the Company s Series C convertible preferred stock with an exercise price of $8.79 per share. The estimated fair value of the warrants issued with the 2012 Notes at issuance was $1.4 million (the 2012 Warrant Liability). The Company estimated the fair value of the 2012 Warrant Liability at issuance utilizing the Black-Scholes-Merton option-pricing model. The 2012 Warrant Liability was revalued at each reporting date with changes in fair value being recognized in change in fair value of convertible preferred stock warrant liability in the accompanying statements of operations (see Note 6). 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.

2013 Notes Payable

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 with several investors and the Company s chief executive officer (the 2013 Notes).

In connection with the issuance of the 2013 Notes, the Company issued warrants which were convertible into either Series B convertible preferred stock or the next series of preferred stock issued. Thus the number of shares was not determinable at the date of issuance. The estimated fair value of the warrants issued with the 2013 Notes was $0.6 million at issuance (the 2013 Warrant Liability). The 2013 Warrant Liability was revalued at each reporting date with changes in fair value being recognized in change in fair value of convertible preferred stock warrant liability in the accompanying statements of operations (see Note 6). 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.

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Otonomy, Inc.,

Notes to Financial Statements (Continued)

(information as of September 30, 2014 and for the nine months ended

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Warrants

As of December 31, 2012 and 2013, the Company s outstanding convertible preferred stock warrants, issued in connection with its convertible notes payable, consisted of the following:

Issue Date	Series	Exercise Price	Number of Shares Outstanding Underlying Warrant	Expiration Date
11/4/2008	Series A	$ 31.0920	14,106	11/4/2018
12/8/2008	Series A	$ 31.0920	14,106	12/8/2018
1/14/2009	Series A	$ 31.0920	14,106	1/14/2019
4/13/2009	Series A	$ 31.0920	14,106	4/13/2019
7/1/2009	Series A	$ 31.0920	14,106	7/1/2019
10/8/2009	Series A	$ 31.0920	14,106	10/8/2019
12/15/2009	Series A	$ 31.0920	14,106	12/15/2019
1/22/2010	Series A	$ 31.0920	14,106	1/22/2020
3/15/2010	Series A	$ 31.0920	703	3/15/2020
4/1/2010	Series A	$ 31.0920	14,106	4/1/2020
5/28/2010	Series A	$ 31.0920	14,456	5/28/2020
8/23/2012	Series C	$ 8.79	182,022	8/23/2022
10/24/2012	Series C	$ 8.79	60	10/24/2022
Total outstanding at December 31, 2012			324,195	
1/22/2013	Series C	$ 8.79	159,322	1/22/2023
Total outstanding at December 31, 2013			483,517	

The aggregate fair value of the Series A and Series C convertible preferred stock warrants as of December 31, 2012 was approximately $1.6 million and $1.3 million, respectively. 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.

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 September 30, 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.

Credit Facility

In July 2013, the Company entered into a loan and security agreement (the Credit Facility) with a bank for working capital in an aggregate principal amount of $7.0 million. In connection with the Credit Facility, the Company granted a security interest in all its assets, except intellectual property. The Company issued a warrant for its Series C convertible preferred stock that would become exercisable for 3% of the amount of the debt actually drawn at an exercise price of $0.25 per share. The Credit Facility and related warrant expired on July 31, 2014. No amounts were drawn under the Credit Facility and there was no debt issued or warrants exercisable.

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Otonomy, Inc.,

Notes to Financial Statements (Continued)

(information as of September 30, 2014 and for the nine months ended

September 30, 2013 and 2014 is unaudited)

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,		Nine Months Ended September 30,	
	2012	2013	2013	2014
			(unaudited)	
Stated interest on convertible notes payable	$ 228	$ 749	$ 749	$
Amortization of deferred financing costs associated with the convertible preferred stock warrants	216	1,779	1,775	39
Total interest expense	$ 444	$ 2,528	$ 2,524	$ 39

5. 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 (see Note 9).

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.

Rent expense for each of the years ended December 31, 2012 and 2013, was $0.4 million. Rent expense was $0.3 million for each of the nine months ended September 30, 2013 and 2014. 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, 2013, future minimum annual obligations under all non-cancellable operating lease commitments, including the facility lease described above are as follows (in thousands):

2014	$ 471
2015	473
2016	487
2017	82
Total	$ 1,513

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, 2013 or September 30, 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,

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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,		Nine Months Ended September 30,	
	2012	2013	2013	2014
			(unaudited)	
License and other fees	$ 25	$ 250	$ 44	$ 19
Milestone fees		1,100	100	
Total license and related fees	$ 25	$ 1,350	$ 144	$ 19

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.

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, 2013 and September 30, 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.

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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.

6. 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.

At December 31, 2012 and 2013, Level 3 liabilities consisted of convertible preferred stock warrant liabilities. The Company held no financial assets or liabilities measured at fair value on a recurring basis as of September 30, 2014. The following fair value hierarchy tables present information about each major category of the Company s financial liabilities measured at fair value on a recurring basis as of December 31, 2012 and 2013 (in thousands):

	Fair Value Measurement at December 31, 2012			
	Fair Value	Level 1	Level 2	Level 3
Liabilities:				
Convertible preferred stock warrants[1]	$ 2,909	$	$	$ 2,909
Total liabilities	$ 2,909	$	$	$ 2,909

(1) Convertible preferred stock warrant liabilities to purchase Series A and Series C convertible preferred stock at December 31, 2012 are classified as Level 3 and were measured at fair value using the Black-Scholes-Merton option pricing model. The Company developed its estimates based on publicly available historical data and all available information as of the valuation date. Inputs used in the pricing model include estimates of the Company s risk-free interest rate, expected dividend yield, expected volatility and expected term. As of December 31, 2012, the warrants were revalued using the Black-Scholes-Merton option pricing model based on the following inputs:

	Series A	Series C
Risk-free interest rate	1.2%	1.8%
Expected dividend yield	0%	0%
Expected volatility	92.2%	88.2%
Expected term (in years)	6.6	9.7

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	Fair Value Measurement at December 31, 2013			
	Fair Value	Level 1	Level 2	Level 3
Liabilities:				
Convertible preferred stock warrants[2]	$ 646	$	$	$ 646
Total liabilities	$ 646	$	$	$ 646

(2) Convertible preferred stock warrant liabilities to purchase Series A and Series C convertible preferred stock at December 31, 2013 are classified as Level 3 and are measured using a hybrid of the option pricing model and the PWERM on each reporting date. The key inputs into the models include the probability and timing of expected liquidity events, discount rates and the selection of appropriate market-comparable transactions and multiples to apply to the Company s various historical and forecasted operational metrics.

The following table provides a reconciliation of all liabilities measured at fair value using Level 3 significant unobservable inputs (in thousands):

	Convertible Preferred Stock Warrant Liability[1]	Convertible Preferred Stock Purchase Right[2]
Balance at December 31, 2011	$ 1,632	$ 3,707
Expiration of convertible preferred stock purchase right		(3,707)
Issuance of convertible preferred stock warrants	1,377	
Change in fair value	(100)	
Balance at December 31, 2012	2,909	
Issuance of convertible preferred stock warrants	570	
Change in fair value	(2,833)	
Balance at December 31, 2013	646	
Change in fair value (unaudited)	3,300	
Reclassification to additional paid-in capital upon closing of IPO	(3,946)	

(unaudited)

Balance at September 30, 2014 (unaudited)	$	$

(1) Changes in the fair value of the convertible preferred stock warrant liability were recognized in change in fair value of convertible preferred stock warrant liability in the accompanying statements of operations.
(2) The change in the fair value of the convertible preferred stock purchase right was recognized in change in fair value of convertible preferred stock purchase right in the accompanying statements of operations.

Convertible Preferred Stock Purchase Right

The convertible preferred stock purchase right (the Purchase Right) was recorded as a liability in accordance with the accounting guidance at its estimated fair value on the date of issuance of $3.8 million, and was revalued at each reporting date for any changes in the estimated fair value.

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The estimated fair value of the Purchase Right was determined using a valuation model that considers the probability of achieving a milestone, the entity s cost of capital, the estimated time period the Purchase Right will be outstanding, consideration received for the instrument with the Purchase Right, the number of shares to be issued and specific share pricing to satisfy the Purchase Right, and any changes in the fair value of the underlying instrument to the Purchase Right. The second closing of the Series B convertible preferred stock financing was completed on May 18, 2011, at which time 996,382 shares of Series B convertible preferred stock were purchased and the related portion of the fair value of the Purchase Right of $1.2 million was reclassified to Series B convertible preferred stock in the accompanying balance sheets. The Purchase Right related to the third tranche expired in June 2012, at which time the carrying value of the liability of $3.7 million was recognized in change in fair value of convertible preferred purchase right in the accompanying statements of operations.

7. Convertible Preferred Stock and Stockholders (Deficit) Equity

Convertible Preferred Stock

Series A Convertible Preferred Stock

In May 2010, the Company entered into an agreement with two investors for the purchase of Series A convertible preferred stock at $31.092 per share. The Company issued 339,863 shares of Series A convertible preferred stock upon the conversion of the Notes and related accrued interest totaling $10.6 million (see Note 4).

Series B Convertible Preferred Stock

In August 2010, the Company entered into an agreement with several investors for the purchase of 1,708,076 shares of the Company s Series B convertible preferred stock to be completed in three closings. The Company issued 708,030 shares of Series B convertible preferred stock at $14.1766 per share for $10.0 million in cash. The Company evaluated the purchase right associated with the second and third tranche closings of the Series B convertible preferred stock and determined that since the purchase right was separately transferrable, the purchase right was therefore a freestanding financial instrument which required separate accounting treatment (see Note 6).

In February 2011, the Company completed a special closing of the Series B convertible preferred stock through the sale of 3,664 shares of Series B convertible preferred stock at $14.1766 per share for net proceeds of approximately $0.1 million in cash.

In May 2011, the Company completed a scheduled second closing of its Series B convertible preferred stock through the sale of 996,382 shares Series B convertible preferred stock at $14.1766 per share for net proceeds of $14.1 million in cash.

Series C Convertible Preferred Stock

In August 2013, the Company entered into a stock purchase agreement with investors for the purchase of 7,040,026 shares of Series C convertible preferred stock at $8.79 per share, to be completed in two closings. The Company issued 4,420,577 shares in the first closing for net proceeds of $22.6 million in cash, plus the conversion of secured convertible promissory notes totaling approximately $16.0 million, including principal and accrued interest. The Company evaluated the purchase right associated with the second tranche of the Series C convertible preferred stock and determined that it was an embedded derivative which did not require separate accounting treatment as the purchase right was not separately transferable.

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In September 2013, the Company completed a special closing of its Series C convertible preferred stock through the sale of 8,532 shares of Series C convertible preferred stock at $8.79 per share for net proceeds of $0.1 million.

In December 2013, the Company completed a second closing of its Series C convertible preferred stock through the sale of 2,610,917 shares of Series C convertible preferred stock at $8.79 per share for net proceeds of $22.9 million.

Series D Convertible Preferred Stock

On April 23, 2014, the Company completed the sale of 4,126,080 shares of Series D convertible preferred stock to new and existing investors at $11.96 per share for net cash proceeds of $49.2 million (see Note 11).

The designated, issued and outstanding shares of convertible preferred stock by series as of December 31, 2012 are as follows (liquidation preference in thousands):

	Shares Designated	Shares Outstanding	Common Stock Equivalents	Liquidation Preference
Series A	406,712	339,863	745,387	$ 13,209
Series B	3,168,373	1,708,076	1,708,076	36,322
	3,575,085	2,047,939	2,453,463	$ 49,531

The designated, issued and outstanding shares of convertible preferred stock by series as of December 31, 2013 are as follows (liquidation preference in thousands):

	Shares Designated	Shares Outstanding	Common Stock Equivalents	Liquidation Preference
Series A	404,671	339,863	745,387	$ 2,987
Series B	1,708,076	1,708,076	1,708,076	15,014
Series C	7,407,062	7,040,026	7,040,026	92,823
	9,519,809	9,087,965	9,493,489	$ 110,824

In connection with the IPO, all of the Company s outstanding shares of convertible preferred stock were automatically converted into shares of common stock. No preferred stock dividends were ever paid or declared by the Company.

Dividends

The holders of the Series C convertible preferred stock are entitled to receive annual noncumulative dividends at a rate of 8% of the original Series C issuance price per annum. The Series C convertible preferred stock dividends are payable when and if declared by the Company s Board of Directors and are payable in preference and in priority to any dividends on the Series B convertible preferred stock, Series A convertible preferred stock and common stock. The holders of the Series B convertible preferred stock are entitled to receive

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annual noncumulative dividends at a rate of 8% of the original Series B issuance price per annum. The Series B convertible preferred stock dividends are payable when and if declared by the Company s Board of Directors and are payable in preference and in priority to any dividends on the Series A convertible preferred stock and common stock. The holders of the Series A convertible preferred stock are entitled to receive annual noncumulative dividends at a rate of 8% of the original Series A issuance price per annum. The Series A convertible preferred stock dividends are payable when and if declared by the Company s Board of Directors. The Series A convertible preferred stock dividends are payable in preference and in priority to any dividends on common stock (see Note 11).

Liquidation Preferences

In August 2013, in connection with the Company s Series C convertible preferred stock financing, the Company amended its certificate of incorporation. Prior to the issuance of the Series C convertible preferred stock, the liquidation preferences on the Series A convertible preferred stock and the Series B convertible preferred stock were approximately $38.8659 and $21.2648 per share, respectively. Subsequent to the Series C convertible preferred stock financing, the liquidation preferences are described below.

Prior to any payment to the holders of the Series B convertible preferred stock, Series A convertible preferred stock and common stock, the holders of the Series C convertible preferred stock are entitled to receive a liquidation preference equal to $13.185 per share, subject to certain anti-dilution adjustments, plus all declared but unpaid dividends on the Series C convertible preferred stock. Prior to any payment to the holders of the Series A convertible preferred stock and common stock, the holders of the Series B convertible preferred stock are entitled to receive a liquidation preference equal to $8.79 per share, subject to certain anti-dilution adjustments, plus all declared but unpaid dividends on the Series B convertible preferred stock. The holders of the Series A convertible preferred stock are entitled to receive a liquidation preference equal to $8.79 per share, subject to certain anti-dilution adjustments, plus all declared but unpaid dividends on the Series A convertible preferred stock. Liquidation payments to the holders of Series A convertible preferred stock have priority and are made in preference to any payments to the holders of common stock. After payment of the full liquidation preferences of the convertible preferred stock, the remaining assets, if any, will be distributed to the holders of the common stock and preferred stock (on an as-if-converted to common stock basis); provided, however that the aggregate amount per share which a holder of a share of convertible preferred stock shall receive shall not exceed $26.37 per share (see Note 11).

Conversion

The shares of Series A convertible preferred stock are convertible into shares of common stock at a ratio of 1:2.193204365 at the option of the holder, subject to certain anti-dilution and other adjustments. The shares of Series B convertible preferred stock and Series C convertible preferred stock are convertible into shares of common stock at a ratio of 1:1 at the option of the holder, subject to certain anti-dilution and other adjustments. Each share of convertible preferred stock is automatically converted into common stock immediately upon: (i) the Company s sale of

its common stock in a firm commitment underwritten public offering pursuant to a registration statement under the Securities Act of 1933, as amended, in which the per share price is at least $43.95 (as adjusted) and the net cash proceeds are at least $75,000,000 or (ii) upon the written consent of the holders of at least 64% of the then outstanding Series C convertible preferred stock (the Requisite Holders) (see Note 11).

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Redemption

At any time following the sixth anniversary of the date the first share of Series C convertible preferred stock was issued (see Note 11), if requested in writing by the Requisite Holders, the Company shall, to the extent it may lawfully do so, redeem all of the outstanding Series A convertible preferred stock, Series B convertible preferred stock and Series C convertible preferred stock in two equal annual installments to be made on both the date that is 60 days following the date of the Requisite Holders written request and on the one-year anniversary following the date of the Requisite Holders written request.

The Company is accreting the issuance costs of the convertible preferred stock and the convertible preferred stock purchase right up to the redemption amount using the effective interest rate method. The Company does not have any redemption requirements until 2019. The aggregate amount of redemption requirements for all series of convertible preferred stock outstanding, excluding warrants, that are potentially redeemable assuming exercise of redemption rights at the earliest possible date, is $79.8 million of which $39.9 million is redeemable in each of the years ending December 31, 2019 and 2020 (see Note 11).

Voting Rights

The preferred stockholders have voting rights equal to the number of common shares they would own upon conversion of their shares of convertible preferred stock, which is currently at a ratio of 2.193204365 shares of common stock to one share of Series A convertible preferred stock for the Series A preferred stockholders and at a one for one ratio into common stock for the Series B and Series C preferred stockholders (see Note 11).

Common Stock Subject to Repurchase

During 2009, the Company sold 11,621 shares of restricted common stock to consultants and employees for $0.001 per share. The common shares generally vest 25% after one year and then monthly over the following three years. As of December 31, 2012, 10,828 of these shares were vested. As of December 31, 2013 and September 30, 2014, all of these shares were vested.

The Company s 2010 Equity Incentive Plan (the 2010 Plan), allows for early exercise of certain option awards issued under the plan. As of December 31, 2012 and 2013, no options had been early exercised. As of September 30, 2014, options had been exercised for the purchase of 16,294 shares of common stock, which were unvested and subject to repurchase. Under the authoritative guidance, early exercise is not considered an exercise for accounting purposes and, therefore, any payment for unvested shares is recognized as a liability at the original exercise price. As of September 30, 2014, the Company has recorded an early exercise liability of $54,000 and no shares have been repurchased by the Company.

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Common Stock Reserved for Future Issuance

Common stock reserved for future issuance is as follows in common equivalent shares:

	December 31, 2013	September 30, 2014
Conversion of convertible preferred stock	9,493,489	
Warrants for the purchase of convertible preferred stock	483,517	
Warrants for the purchase of common stock		142,113
Common stock options issued and outstanding	1,235,705	2,058,910
Common stock options available for future grant	537,993	2,602,675
Common stock reserved for issuance under ESPP		380,000
Total common stock reserved for future issuance	11,750,704	5,183,698

8. Stock Compensation Plans

2010 Equity Incentive Plan

The Company granted awards under the 2010 Plan until June 2014. The terms of the 2010 Plan provide for the grant of incentive stock options to the Company s employees and any parent and subsidiary corporations employees, and for the grant of nonstatutory stock options, restricted stock, restricted stock units and stock appreciation rights to the Company s employees, directors and consultants, and the Company s parent and subsidiary corporations employees and consultants. The compensation committee of the board of directors had the authority to approve the employees and other service providers to whom equity awards were granted and had the authority to determine the terms of each award, subject to the terms of the 2010 Plan, including (i) the number of shares of common stock subject to the award; (ii) when the award becomes exercisable; (iii) the option or stock appreciation right exercise price, which must be at least 100% of the fair market value of the common stock as of the date of grant; and (iv) the duration of the option or stock appreciation right (which may not exceed 10 years). Options granted under the 2010 Plan generally are scheduled to vest over four years, subject to continued service, and subject to certain acceleration of vesting

provisions, and expire no later than 10 years from the date of grant. In connection with the adoption of the 2014 Equity Incentive Plan, the Company terminated the 2010 Plan for future use and provided that no further equity awards are to be granted under the 2010 Plan. All outstanding awards under the 2010 Plan will continue to be governed by their existing terms.

2014 Equity Incentive Plan

In July 2014, the Company s board of directors adopted and the Company s stockholders approved a 2014 Equity Incentive Plan (the 2014 Plan), and the 2014 Plan became effective August 11, 2014. The 2014 Plan permits the grant of incentive stock options to the Company s employees and any parent and subsidiary corporations employees, and for the grant of nonstatutory stock options, restricted stock, restricted stock units, stock appreciation rights, performance units and performance shares to the Company s employees, directors and consultants and the Company s parent and subsidiary corporations employees and consultants.

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Upon adoption of the 2014 Plan, a total of 2,606,875 shares of common stock were reserved for issuance, including 386,875 shares of common stock previously available for issuance under the 2010 Plan. In addition, the shares to be reserved for issuance under the 2014 Plan will also include shares subject to stock options or similar awards granted under the 2010 Plan that expire or terminate without having been exercised in full and shares issued pursuant to awards granted under the Company s 2010 Plan that are forfeited to or repurchased by the Company.

The number of shares available for issuance under the 2014 Plan will also include an annual increase on the first day of each fiscal year beginning in 2015, equal to the least of (i) 2,500,000 shares; (ii) 5% of the outstanding shares of common stock as of the last day of the immediately preceding fiscal year; or (iii) such other amount as the Company s board of directors may determine.

The compensation committee of the board of directors has the authority to approve the employees and other service providers to whom equity awards are granted and to determine the terms of each award, subject to the terms of the 2014 Plan. The compensation committee may determine the number of shares subject to an award, except that the 2014 Plan provides certain limits on the number of awards that may be granted to non-employee members of the board of directors under the 2014 Plan in any fiscal year. Options and stock appreciation rights granted under the 2014 Plan must have a per share exercise price equal to at least 100% of the fair market value of a shares of the common stock as of the date of grant and may not expire later than 10 years from the date of grant.

As of December 31, 2013, 537,993 options were available for grant under the 2010 Plan. As of September 30, 2014, 2,602,675 options were available for grant under the 2014 Plan. The following table summarizes stock option activity for the year ended December 31, 2013 and for the nine months ended September 30, 2014 (in thousands except per share amounts and years):

	Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (In Years)	Aggregate Intrinsic Value
Outstanding as of December 31, 2012	383	$ 2.75		
Granted	862	$ 1.76		
Exercised	(2)	$ 3.17		
Forfeited	(7)	$ 2.71		
Outstanding as of December 31, 2013	1,236	$ 2.06	9.2	$ 47
Granted	884	$ 5.47		

Exercised	(61)	$ 2.51			
Outstanding as of September 30, 2014	2,059	$ 3.51	8.9	$	42,189
Options vested and expected to vest as of December 31, 2013	1,207	$ 2.06	9.2	$	47
Options exercisable as of December 31, 2013	505	$ 2.46	8.4	$	15
Options vested and expected to vest as of September 30, 2014	2,028	$ 3.46	9.0	$	41,659
Options exercisable as of September 30, 2014	910	$ 3.38	7.4	$	18,761

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

	Years Ended December 31,		Nine Months Ended September 30,	
	2012	2013	2013	2014
			(unaudited)	
Weighted-average grant date fair value per share of options granted during the period	$ 0.79	$ 1.28	$	$ 3.85
Fair value of options vested during the period	194	206	137	502
Cash received from options exercised during the period[(1)]	3	5	5	153
Intrinsic value of options exercised during the period				111

(1) For the nine months ended September 30, 2014, cash received from options exercised during the period includes cash proceeds of $54,000 for shares which were early exercised and subject to repurchase as of September 30, 2014. The Company has reflected the early exercise liability within accrued expenses in the accompanying balance sheets.

2014 Employee Stock Purchase Plan

In July 2014, the Company s board of directors adopted and the stockholders approved the Company s 2014 Employee Stock Purchase Plan (the ESPP), which became effective upon adoption by the Company s board of directors. The ESPP allows eligible employees to purchase shares of the Company s common stock at a discount through payroll deductions of up to 15% of their eligible compensation, subject to any plan limitations. The offering periods generally start on the first trading day on or after June 1 and December 1 of each year and end on the first trading day on or before June 1 and December 1 approximately twenty-four months later, and will include six-month purchase periods. The administrator may, in its discretion, modify the terms of future offering periods. Due to the timing of our initial public offering, the first offering period started on August 12, 2014 and will end on June 1, 2016.

The ESPP initially authorized the issuance of 380,000 shares of the Company s common stock pursuant to rights granted to employees for their payroll deductions. The number of shares available for issuance under the ESPP will also include an annual increase on the first day of each fiscal year beginning in 2015, equal to the least of (i) 800,000 shares; (ii) 1.5% of the outstanding shares of common stock as of the last day of the immediately preceding fiscal year; or (iii) such other amount as the Company s board of directors may determine.

Through September 30, 2014, no shares of common stock have been issued pursuant to ESPP purchases.

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Stock-Based Compensation Expense

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

	Years Ended December 31,		Nine Months Ended September 30,	
	2012	2013	2013[1]	2014
			(unaudited)	
Risk-free interest rate	1.0%	2.0%		1.9%
Expected dividend yield	0.0%	0.0%		0.0%
Expected volatility	92.2%	85.5%		82.3%
Expected term (in years)	6.1	6.1		6.1

(1) The Company did not issue any stock options during the nine months ended September 30, 2013.

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

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

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

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

Forfeitures. The Company reduces stock-based compensation expense for estimated forfeitures. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

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

	Years Ended December 31,		Nine Months Ended September 30,	
	2012	2013	2013	2014
			(unaudited)	
Research and development	$ 78	$ 62	$ 40	$ 407
General and administrative	113	121	85	488
Total stock-based compensation	$ 191	$ 183	$ 125	$ 895

As of December 31, 2013, total compensation costs related to non-vested stock options not yet recognized is $1.3 million which is expected to be recognized over a remaining weighted-average vesting period of 3.3 years.

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As of September 30, 2014, total compensation costs related to non-vested stock options not yet recognized is $3.9 million which is expected to be recognized over a remaining weighted-average vesting period of 3.5 years.

9. Related Party Transactions

The Company has entered into various services agreements with affiliates of a principal stockholder. Under the terms of the agreements, the affiliated companies shared common services, such as accounting and finance support, through December 2013, and shared facilities through June 2012.

The following table summarizes related party receivables, payables, payments made and expenses related to affiliated companies under these agreements (in thousands):

	Years Ended December 31,		Nine Months Ended September 30,	
	2012	2013	2013	2014
			(unaudited)	
Receivable	$ 17	$ 9	$ 12	$
Payable	6	10	5	
Payments	79	28	14	10
Expenses	60	32	15	

10. Income Taxes

Pursuant to Internal Revenue Code (IRC) Sections 382 and 383, annual use of the Company s net operating loss and research and development credit carryforwards may be limited in the event that a cumulative change in ownership of more than 50% occurs within a three-year period. The Company has completed an IRC Section 382/383 analysis, regarding the limitation of net operating loss and research and development credit carryforwards as of December 31, 2013. As a result of the analysis, two ownership changes were determined to have occurred. Based on these changes, the deferred tax assets for net operating losses and federal research and development credits of $3.2 million and $0.3 million, respectively, have been removed from the deferred tax asset schedule and the Company has recorded a corresponding decrease in the valuation allowance. The California research and development credits were not limited as these credits carry forward indefinitely. The Company will continue to consider changes in ownership that may cause losses of tax attributes in the future.

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Otonomy, Inc.,

Notes to Financial Statements (Continued)

(information as of September 30, 2014 and for the nine months ended

September 30, 2013 and 2014 is unaudited)

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

	December 31,	
	2012	**2013**
Deferred tax assets:		
Net operating loss carryforwards	$ 11,252	$ 18,620
Research and development credits	621	1,363
Depreciation and amortization	433	906
Accrued expenses	75	76
Deferred rent	126	116
Other, net	27	31
Total deferred tax assets	12,534	21,112
Less: valuation allowance	(12,534)	(21,112)
Total	$	$

Due to the Company s history of losses and uncertainty regarding future earnings, a full valuation allowance has been recorded against the Company s deferred tax assets, as it is more likely than not that such assets will not be realized. A valuation allowance of approximately $12.5 million and $21.1 million has been established as of December 31, 2012 and 2013, respectively.

At December 31, 2013, the Company had federal and California net operating loss carryforwards of approximately $46.8 million and $46.6 million, respectively, net of IRC Section 382 limitations. The federal and California net operating loss carryforwards will begin to expire in 2030, unless previously utilized. At December 31, 2013, the Company also had federal and California research and development credit carryforwards of approximately $1.6 million net of IRC Section 383 limitations and $1.1 million, respectively. The federal research and development credit carryforwards will begin expiring in 2030 unless previously utilized. The California research credit will carry forward indefinitely.

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

	2012	**2013**

Federal statutory rate	$ (2,573)	$ (6,650)
State tax (net of federal benefit)	(628)	(1,148)
Permanent items, other	56	65
Change in fair value of convertible preferred stock warrant liability	(1,260)	(963)
Change in fair value of convertible preferred stock purchase right	(34)	
Non-deductible interest	150	855
Other adjustments	10	91
Research and development credits	(160)	(1,236)
Uncertain tax positions	60	409
Change in valuation allowance	4,380	8,578
Provision for income taxes	$ 1	$ 1

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Otonomy, Inc.,

Notes to Financial Statements (Continued)

(information as of September 30, 2014 and for the nine months ended

September 30, 2013 and 2014 is unaudited)

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

	December 31,	
	2012	**2013**
Balance at the beginning of the year	$ 422	$ 515
Adjustments related to prior year tax positions	(4)	136
Increases related to current year tax positions	97	406
Decreases due to statute of limitations expiration		
Decreases due to IRC Section 382/383 limitation		
	$ 515	$ 1,057

The Company s policy is to include interest and penalties related to unrecognized income tax benefits as a component of income tax expense. The Company has no accruals for interest or penalties in the accompanying balance sheets as of December 31, 2012 and 2013 and has not recognized interest or penalties in the accompanying statements of operations for the years ended December 31, 2012 and 2013.

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

The Company is subject to taxation in the United States and California. Due to the net operating loss carryforwards, the U.S. federal and state returns are open to examination by the IRS and California for all years since inception. The Company has not been, nor is it currently, under examination by the federal or any state tax authority.

11. Subsequent Events

The Company evaluated all events or transactions that occurred after the balance sheet date of December 31, 2013 through June 5, 2014, the date on which these financial statements were available to be issued.

Series D Convertible Preferred Stock

On April 23, 2014, the Company completed the sale of 4,126,080 shares of Series D convertible preferred stock to new and existing investors at $11.96 per share for net cash proceeds of $49.2 million.

Amended Certificate of Incorporation in Connection with the Issuance of the Series D Convertible Preferred Stock

The certificate of incorporation as amended immediately prior to the issuance of the Series D convertible preferred stock is described below.

The holders of the Series C and Series D convertible preferred stock on a pari passu basis and in priority have preference to the holders of the Series B and Series A convertible preferred stock and the holders of common stock. The holders of the Series B convertible preferred stock have priority over the holders of Series A convertible preferred stock and the holders of common stock.

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Otonomy, Inc.,

Notes to Financial Statements (Continued)

(information as of September 30, 2014 and for the nine months ended

September 30, 2013 and 2014 is unaudited)

After payment of the liquidation preferences, the remaining assets, if any, will be distributed to the holders of the common stock and the Series B, Series C and Series D convertible preferred stock on a pro rata basis. Each share of convertible preferred stock is automatically converted into common stock immediately upon (i) the Company s sale of its common stock in a firm commitment underwritten public offering pursuant to a registration statement under the Securities Act of 1933, as amended, in which the per share price is at least $35.87 (as adjusted) and the net cash proceeds are at least $70,000,000 or (ii) upon the written consent of 75% of the then outstanding Preferred Stock on an as-converted basis (the Preferred Stockholders).

The following table summarizes the preferred stock preferences in connection with the issuance of the Series D convertible preferred stock:

	Dividend Rate	Conversion Rate	Liquidation Preference Per Share
Series D	8%	1:1	$ 11.96
Series C	8%	1:1	8.79
Series B	8%	1:1	8.79
Series A	8%	1:2.193204365	31.092

At any time following the sixth anniversary of the date the first share of Series D convertible preferred stock was issued, if requested in writing by the Preferred Stockholders, the Company shall, to the extent it may lawfully do so, redeem all of the outstanding Series A convertible preferred stock, Series B convertible preferred stock, Series C convertible preferred stock and Series D convertible preferred stock in two equal annual installments to be made on both the date that is 60 days following the date of the Preferred Stockholders written request and on the one-year anniversary following the date of the Preferred Stockholders written request.

The Company is accreting the issuance costs of the convertible preferred stock and the convertible preferred stock purchase right up to the redemption amount using the effective interest rate method. The Company does not have any redemption requirements until 2020. The aggregate amount of redemption requirements for all series of convertible preferred stock outstanding, excluding warrants that are potentially redeemable assuming exercise of redemption rights at the earliest possible date is $136.8 million, of which $68.4 million is redeemable in each of the years ending December 31, 2020 and 2021.

The preferred stockholders have voting rights equal to the number of common shares they would own upon conversion of their shares of convertible preferred stock, which is currently at a ratio of 2.193204365 shares of common stock to one share of Series A convertible preferred stock for the Series A preferred stockholders and at a one-for-one ratio into common stock for the Series B, Series C and Series D preferred stockholders.

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.

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Shares

Common Stock

J.P. Morgan

Piper Jaffray **Cowen and Company**

Sanford C. Bernstein

, 2015

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PART II

INFORMATION NOT REQUIRED IN THE PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution.

Estimated expenses, other than underwriting discounts and commissions, payable by the Registrant in connection with the sale of the common stock being registered under this registration statement are as follows:

	Amount to be Paid
SEC registration fee	$ 10,023
FINRA filing fee	$ 13,438
Printing and engraving expenses	*
Legal fees and expenses	*
Accounting fees and expenses	*
Transfer agent and registrar fees and expenses	*
Miscellaneous expenses	*
Total	$ *

*To be filed by amendment.

Item 14. Indemnification of Directors and Officers.

The Registrant s amended and restated certificate of incorporation contains provisions that eliminate, to the maximum extent permitted by the General Corporation Law of the State of Delaware, the personal liability of the Registrant s directors and executive officers for monetary damages for breach of their fiduciary duties as directors or officers. The Registrant s amended and restated certificate of incorporation and bylaws provide that the Registrant must indemnify its directors and executive officers and may indemnify its employees and other agents to the fullest extent permitted by the General Corporation Law of the State of Delaware.

Sections 145 and 102(b)(7) of the General Corporation Law of the State of Delaware provide that a corporation may indemnify any person made a party to an action by reason of the fact that he or she was a director, executive officer, employee or agent of the corporation or is or was serving at the request of a corporation against expenses (including attorneys fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by him or her in connection with such action if he or she acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, the best interests of the corporation and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful, except that, in the case of an action by or in right of the corporation, no indemnification may generally be made in respect of any claim as to which such person is adjudged to be liable to the corporation.

The Registrant has entered into indemnification agreements with its directors and executive officers, in addition to the indemnification provided for in its amended and restated certificate of incorporation and bylaws, and intends to enter

into indemnification agreements with any new directors and executive officers in the future.

The Registrant has purchased and currently intends to maintain insurance on behalf of each and any person who is or was a director or officer of the Registrant against any loss arising from any claim asserted against him or her and incurred by him or her in any such capacity, subject to certain exclusions.

The Underwriting Agreement (Exhibit 1.1 hereto) provides for indemnification by the underwriters of the Registrant and its executive officers and directors, and by the Registrant of the underwriters, for certain liabilities, including liabilities arising under the Securities Act.

See also the undertakings set out in response to Item 17 herein.

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Item 15. Recent Sales of Unregistered Securities.

Since January 1, 2012, the Registrant has issued and sold the following unregistered securities:

(1) On April 23, 2014, the Registrant issued and sold 4,126,080 shares of its series D convertible preferred stock in a private placement to accredited investors at a purchase price per share of $11.96 for gross proceeds of approximately $49.3 million.

(2) Between August 26, 2013 and December 17, 2013, the Registrant issued and sold an aggregate of 7,040,026 shares of its series C convertible preferred stock in a private placement to accredited investors at a purchase price per share of $8.79, for aggregate consideration of approximately $61.9 million. Of this amount, $16.0 million was paid for by cancellation of principal and accrued interest under the secured convertible promissory notes described in paragraph (5) below.

(3) On July 31, 2013, the Registrant issued and sold a warrant to purchase up to a maximum of 23,890 shares of series C convertible preferred stock with an exercise price per share of $8.79 to Square 1 Bank in connection with a credit facility. Such warrant expired on July 31, 2014, with no shares exercisable thereunder.

(4) Between August 23, 2012 and January 22, 2013, the Registrant issued and sold warrants to purchase an aggregate of 341,404 shares of its series C convertible preferred stock at an exercise price per share of $8.79 to certain of its series C investors. These warrants were issued in connection with the sale and issuance of the secured convertible promissory notes described in paragraph (5) below.

(5) Between August 23, 2012 and January 22, 2013, the Registrant issued secured convertible promissory notes in the aggregate principal amount of $15.0 million. These notes converted into 1,818,191 shares of the Registrant s series C convertible preferred stock in August 26, 2013 as described in paragraph (2) above.

(6) Between January 1, 2012 and August 13, 2014, the Registrant granted to its directors, employees, consultants and other service providers options to purchase an aggregate of 1,812,529 shares of common stock under the Registrant s 2010 Equity Incentive Plan (2010 Plan) at exercise prices per share ranging from $1.06 to $6.33, for an aggregate exercise price of approximately $6.3 million.

(7) Between January 1, 2012 and August 13, 2014, the Registrant issued and sold to its directors, employees, consultants and other service providers an aggregate of 60,564 shares of common stock upon the exercise of options under the 2010 Plan at exercise prices per share ranging from $1.06 to $6.33, for an aggregate exercise price of approximately $0.2 million.

None of the foregoing transactions involved any underwriters, underwriting discounts or commissions, or any public offering. The Registrant believes these transactions were exempt from registration under the Securities Act in reliance upon Section 4(a)(2) of the Securities Act or Regulation D, Regulation S or Rule 701 promulgated under the Securities Act as transactions by an issuer not involving any public offering, outside the United States, or pursuant to

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 legends were placed upon the stock certificates issued in these transactions. All recipients had adequate access, through their relationships with us or otherwise, to information about the Registrant.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits.

See the Exhibit Index immediately following the Signature Pages.

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(b) Financial Statement Schedules.

All other schedules have been omitted because the information required to be presented in them is not applicable or is shown in the financial statements or related notes.

Item 17. Undertakings.

The Registrant hereby undertakes to provide to the underwriters at the closing as specified in the underwriting agreement certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended, may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933, as amended, and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933, as amended, and will be governed by the final adjudication of such issue.

The Registrant hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

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SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of San Diego, State of California, on January 8, 2015.

OTONOMY, INC.

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

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints David A. Weber, Ph.D. and Paul E. Cayer and each of them acting individually, as his or her attorneys-in-fact, each with full power of substitution and resubstitution, for him or her in any and all capacities, to sign any and all amendments including post-effective amendments to this Registration Statement and any subsequent registration statement relating to the same offering as this Registration Statement that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act of 1933, as amended, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises hereby ratifying and confirming all that said attorneys-in-fact and agents, or his or her or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated:

Signature	Title	Date
/s/ David A. Weber David A. Weber, Ph.D.	President, Chief Executive Officer and Director *(Principal Executive Officer)*	January 8, 2015
/s/ Paul E. Cayer Paul E. Cayer	Chief Financial and Business Officer, and Secretary *(Principal Financial and Accounting Officer)*	January 8, 2015
/s/ Peter Bisgaard Peter Bisgaard	Chairman of the Board of Directors	January 8, 2015
/s/ Vickie Capps	Director	January 8, 2015

Vickie Capps		
/s/ Brian Dovey	Director	January 8, 2015
Brian Dovey		

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Signature	Title	Date
/s/ Chau Q. Khuong	Director	January 8, 2015
Chau Q. Khuong		
/s/ Jay Lichter	Director	January 8, 2015
Jay Lichter, Ph.D.		
/s/ John P. McKearn	Director	January 8, 2015
John P. McKearn, Ph.D.		
/s/ Heather Preston	Director	January 8, 2015
Heather Preston, M.D.		

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EXHIBIT INDEX

Exhibit Number	Description	Incorporation by Reference			
		Form	File No.	Exhibit	Filing Date
1.1*	Form of Underwriting Agreement, including Form of Lock-up Agreement.				
2.1#	Asset Transfer Agreement between the Registrant and IncuMed, LLC, dated April 30, 2013.	S-1	333-197365	2.1	7/11/2014
3.1	Amended and Restated Certificate of Incorporation of the Registrant.	S-1	333-197365	3.2	8/1/2014
3.2	Amended and Restated Bylaws of the Registrant.	S-1	333-197365	3.4	8/1/2014
4.1	Third Amended and Restated Investors Rights Agreement among the Registrant and certain of its stockholders, dated April 23, 2014.	S-1	333-197365	4.1	7/11/2014
4.2	Specimen common stock certificate of the Registrant.	S-1	333-197365	4.2	7/28/2014
5.1*	Opinion of Wilson Sonsini Goodrich & Rosati, Professional Corporation.				
10.1+	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers.	S-1	333-197365	10.1	8/1/2014
10.2+	Amended and Restated 2010 Equity Incentive Plan and forms of agreement thereunder.	S-1	333-197365	10.2	8/1/2014
10.3+	2014 Equity Incentive Plan and forms of agreements thereunder, to be in effect upon the completion of this offering.	S-1	333-197365	10.3	8/1/2014
10.4+	2014 Employee Stock Purchase Plan and form of agreement thereunder, to be in effect upon the completion of this offering.	S-1	333-197365	10.4	8/1/2014
10.5+	Executive Incentive Compensation Plan, to be in effect upon the completion of this offering.	S-1	333-197365	10.5	7/28/2014
10.6+	Executive Employment Agreement between the Registrant and David A. Weber, Ph.D., dated July 30, 2014.	S-1	333-197365	10.6	8/1/2014
10.7+	Executive Employment Agreement between the Registrant and Paul E. Cayer, dated July 31, 2014.	S-1	333-197365	10.7	8/1/2014
10.8+	Executive Employment Agreement between the Registrant and Carl LeBel, Ph.D., dated July 31,	S-1	333-197365	10.8	8/1/2014

	2014.				
10.9+	Executive Employment Agreement between the Registrant and Robert Michael Savel, II, dated July 31, 2014.	S-1	333-197365	10.9	8/1/2014
10.10+	Executive Employment Agreement between the Registrant and Anthony J. Yost, dated October 20, 2014.				
10.11	Lease Agreement between the Registrant and ARE-SD Region No. 25, LLC, dated September 23, 2011, as amended on May 28, 2014.	S-1	333-197365	10.9	7/11/2014

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Exhibit Number	Description	Incorporation by Reference Form	File No.	Exhibit	Filing Date
10.12	Loan and Security Agreement between the Registrant and Square 1 Bank, dated July 31, 2013.	S-1	333-197365	10.10	7/11/2014
10.13#	License and Commercialization Agreement between the Registrant and DURECT Corporation, dated April 30, 2013.	S-1	333-197365	10.11	7/11/2014
10.14#	License Agreement between the Registrant and The Regents of the University of California, dated November 5, 2008, as amended on January 27, 2010, June 9, 2010 and November 7, 2012.	S-1	333-197365	10.12	7/11/2014
10.15	Form of Warrant to Purchase Series A Convertible Preferred Stock issued pursuant to the Registrant s Note and Warrant Purchase Agreement, dated December 8, 2008.	S-1	333-197365	10.13	7/11/2014
10.16	Form of Warrant to Purchase Shares of Preferred Stock issued pursuant to the Registrant s Note and Warrant Purchase Agreement, dated August 23, 2012.	S-1	333-197365	10.14	7/11/2014
10.17	Warrant to Purchase Stock issued pursuant to Loan and Security Agreement between the Registrant and Square 1 Bank, dated July 31, 2013.	S-1	333-197365	10.15	7/11/2014
23.1	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm.				
23.2*	Consent of Wilson Sonsini Goodrich & Rosati, Professional Corporation (included in Exhibit 5.1).				
24.1	Power of Attorney (included on the signature page of this registration statement on Form S-1).				
101.INS*	XBRL Instance Document.				
101.SCH*	XBRL Taxonomy Extension Schema Document				
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document.				
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document.				
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document.				
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document.				

*To be filed by amendment.

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

+Indicates management contract or compensatory plan.