Otonomy, Inc.
Form S-1/A
January 21, 2015
Table of Contents

As filed with the Securities and Exchange Commission on January 21, 2015.

Registration No. 333-201401

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

AMENDMENT NO. 1

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	$86,636,400	$10,068

(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. Of this amount, $10,023 was previously paid in connection with a prior filing of this Registration Statement.

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.

Table of Contents

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 21, 2015

PRELIMINARY PROSPECTUS

2,150,000 Shares

Common Stock

We are selling 2,150,000 shares of our common stock.

Our common stock is listed on The NASDAQ Global Select Market under the symbol OTIC. On January 20, 2015, the last reported sale price of our common stock on The NASDAQ Global Select Market was $35.04 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 322,500 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

Table of Contents

TABLE OF CONTENTS

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

The Offering

Common stock offered by us	2,150,000 shares
Common stock to be outstanding after this offering	23,322,221 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 322,500 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 322,500 shares of our common stock in this offering.

Table of Contents

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.

Table of Contents

	As of September 30, 2014	
	Actual	As Adjusted[1][2]
	(in thousands) (unaudited)	
Balance Sheet Data:		
Cash	$ 165,155	$ 235,071
Working capital	161,761	231,677
Total assets	168,325	238,241
Accumulated deficit	(92,675)	(92,675)
Total stockholders equity	162,598	232,514

(1) The as adjusted balance sheet data in the table above reflects the sale of 2,150,000 shares of our common stock in this offering and the application of the net proceeds at an assumed public offering price of $35.04 per share, which was the last sale price of our common stock as reported by The NASDAQ Global Select Market on January 20, 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 $35.04 per share would increase (decrease) each of cash, working capital, total assets and total stockholders equity by approximately $2.0 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 $32.9 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.

Table of Contents

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

Table of Contents

$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.

Table of Contents

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.

Table of Contents

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

Table of Contents

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;

Table of Contents

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,

Table of Contents

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

Table of Contents

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.

Table of Contents

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.

Table of Contents

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

Table of Contents

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.

Table of Contents

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.

Table of Contents

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

Table of Contents

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.

Table of Contents

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;

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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

Table of Contents

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.

Table of Contents

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

Table of Contents

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;

Table of Contents

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.

Table of Contents

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.

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 $25.07 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 $35.04 per share, which was the last reported sales price of our common stock on The NASDAQ Global Select Market on January 20, 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 50.9% 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

Table of Contents

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

Table of Contents

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.

Table of Contents

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

Table of Contents

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;