As filed pursuant to Rule 424(b)(5)
Registration No. 333-227269

Prospectus supplement
(To prospectus dated September 21, 2018)

14,500,000 Shares of Common Stock

Pre-Funded Warrants to Purchase 4,000,000 Shares of Common Stock

We are offering 14,500,000 shares of our common stock and, in lieu of common stock to certain investors that so choose, pre-funded warrants to purchase 4,000,000 shares of our common stock pursuant to this prospectus supplement and the accompanying prospectus. The purchase price of each pre-funded warrant equals the price per share at which shares of our common stock are being sold to the public in this offering, minus $0.001, and the exercise price of each pre-funded warrant equals $0.001 per share. This prospectus supplement also relates to the offering of the shares of our common stock issuable upon the exercise of such pre-funded warrants.

Our common stock is quoted on The Nasdaq Global Select Market under the symbol “OTIC.” On July 8, 2020, the last reported sale price of our common stock was $3.56 per share. There is no established public trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on The Nasdaq Global Select Market or any other national securities exchange or nationally recognized trading system.

	Per Share	*Per Pre-Funded Warrant*	*Total*
Public offering price	**$ 3.250000**	**$ 3.249000**	**$ 60,121,000.00**
Underwriting discounts and commissions(1)	**$ 0.203125**	**$ 0.203125**	**$ 3,757,812.50**
Proceeds to Otonomy, Inc., before expenses	**$ 3.046875**	**$ 3.045875**	**$ 56,363,187.50**

(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 2,775,000 additional shares of common stock.

Investing in our securities involves a high degree of risk. See “Risk Factors” beginning on page S-9 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement and the accompanying prospectus are truthful or complete. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares of common stock to purchasers on July 13, 2020. The pre-funded warrants are expected to be delivered on July 13, 2020.

Joint Book-Running Managers

Cowen **Piper Sandler** **Cantor**

Lead Manager

H.C. Wainwright & Co.

July 9, 2020

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and accompanying prospectus relates to the offering of our common stock and pre-funded warrants. Before buying any of the common stock and pre-funded warrants that we are offering, we urge you to carefully read this prospectus supplement, the accompanying prospectus, any free writing prospectus that we have authorized for use in connection with this offering, and the information incorporated by reference as described under the headings “Where You Can Find More Information” and “Information Incorporated by Reference” in this prospectus supplement. These documents contain important information that you should consider when making your investment decision.

This document consists of two parts. The first part is this prospectus supplement, which describes the specific terms of this offering and also adds to, and updates information contained in, the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus, including the documents incorporated by reference into the accompanying prospectus, provides more general information, some of which may not apply to this offering. Generally, when we refer to this prospectus, we are referring to the combined document consisting of this prospectus supplement and the accompanying prospectus. In this prospectus supplement, as permitted by law, we “incorporate by reference” information from other documents that we file with the Securities and Exchange Commission, or the SEC. This means that we can disclose important information to you by referring to those documents. The information incorporated by reference is considered to be a part of this prospectus supplement and the accompanying prospectus and should be read with the same care. When we make future filings with the SEC to update the information contained in documents that have been incorporated by reference, the information included or incorporated by reference in this prospectus supplement is considered to be automatically updated and superseded. In other words, in case of a conflict or inconsistency between information contained in this prospectus supplement and information in the accompanying prospectus or incorporated by reference into this prospectus supplement, you should rely on the information contained in the document that was filed later.

You should rely only on the information contained in, or incorporated by reference into, this prospectus supplement, the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering. Neither we nor the underwriters authorized any other person to provide you with different information. We are not making an offer to sell or soliciting an offer to buy our securities in any jurisdiction in which an offer or solicitation is not authorized or in which the person making that offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations, and prospects may have changed since those dates.

No action is being taken in any jurisdiction outside the United States to permit a public offering of the securities or possession or distribution of this prospectus supplement or the accompanying prospectus in that jurisdiction. Persons who come into possession of this prospectus supplement or the accompanying prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus supplement or the accompanying prospectus applicable to that jurisdiction.

PROSPECTUS SUPPLEMENT SUMMARY

This summary description about us and our business highlights selected information contained elsewhere in this prospectus supplement, the accompanying prospectus, or incorporated in this prospectus supplement by reference. This summary does not contain all of the information you should consider before buying securities in this offering. You should carefully read this entire prospectus supplement and the accompanying prospectus, including each of the documents incorporated herein or therein by reference, before making an investment decision. Unless the context otherwise requires, the terms "Otonomy," "the Company," "we," "us" and "our" in this prospectus supplement and accompanying prospectus refer to Otonomy, Inc.

Overview

We are a biopharmaceutical company dedicated to the development of innovative therapeutics for neurotology. We pioneered the application of drug delivery technology to the ear in order to develop products that achieve sustained drug exposure from a single local administration. This approach is covered by a broad patent estate and has been utilized to develop a pipeline of product candidates including three clinical-stage programs (OTIVIDEX for Ménière's disease, OTO-313 for tinnitus, and OTO-413 for hearing loss) as well as several preclinical development programs including a gene therapy collaboration targeting the most common form of congenital hearing loss**.** We estimate, based on an external market report commissioned by us, that approximately 39 million patients in the United States, suffer from the hearing and balance disorders that we are targeting in our clinical and preclinical programs, including moderate or severe vertigo (approximately 11 million), tinnitus (approximately 8 million) or hearing loss (approximately over 20 million). We also developed, registered and commercialized in the United States an otic antibiotic called OTIPRIO that is being marketed by a co-promotion partner.

OTIVIDEX for Ménière's Disease

OTIVIDEX 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 ear fullness. The underlying cause of Ménière's disease is not well understood and there is no known cure. The typical patient is diagnosed in their 40s and 50s. There are more than 850,000 patients diagnosed with Ménière's disease in the United States, of which approximately 280,000 patients visit physicians during a year**.** There are currently no FDA-approved drug treatments so typical first line treatment in the United States is observance of a low-salt diet and off-label use of diuretics. We estimate that approximately 50% of the Ménière's patients who visit physicians yearly have persistent or severe symptoms that are treated with off-label oral and/or intratympanic (IT) injections of steroids. Patients who are unresponsive to steroid treatment may resort to surgical or chemical ablation, which can cause irreversible hearing loss. Based on an external market analysis commissioned by us, we believe that the total annual U.S. market opportunity for OTIVIDEX in Ménière's disease could exceed $500 million.

In the second half of 2017, we announced the results of two Phase 3 clinical trials for OTIVIDEX in Ménière's disease patients. In November 2017, we announced positive results from the AVERTS-2 trial conducted in Europe. This clinical trial achieved its primary endpoint of count of definitive vertigo days (DVD) using a Generalized Poisson model for OTIVIDEX vs. placebo based on analysis of all 174 Ménière's disease patients enrolled in the trial (p value = 0.029) as well as for the 111 subjects who completed the three-month observation period following treatment (p value = 0.013). For subjects who completed daily diaries through Month 3 (n=105), the OTIVIDEX group demonstrated a 6.2-day

reduction in the mean reported number of DVD from baseline to Month 3 with a 2.5-day mean difference between OTIVIDEX and placebo in Month 3. There was a 68% reduction in vertigo frequency from baseline to Month 3 in the OTIVIDEX group vs. 40% for placebo.

In August 2017, we announced negative results from the AVERTS-1 trial conducted in the United States that enrolled a total of 165 patients with Ménière's disease. The clinical trial missed its primary endpoint, count of DVD using a Generalized Poisson model (p value = 0.62). Patients in both the OTIVIDEX and placebo groups showed similar reductions in the number and severity of vertigo episodes in Month 3 following treatment with OTIVIDEX patients reporting a 58% reduction from baseline in vertigo frequency vs. 55% for placebo patients. We believe that the higher placebo response observed in this trial is attributable to a number of factors including patient expectation bias and have taken steps in the ongoing Phase 3 trial to mitigate these factors. These steps include exclusion of commercially-oriented clinical trial research sites, recruitment of well-characterized Ménière's patients with no advertising, and careful management of clinical site communication with study subjects utilizing placebo response training.

The clinically significant treatment benefit demonstrated by OTIVIDEX versus placebo in AVERTS-2 was consistent with our expectations from the Phase 2b clinical trial. Considering patients from the Phase 2b trial with the same vertigo entry criteria as the Phase 3 trials (4-22 DVD during the baseline month), the OTIVIDEX group demonstrated a 6.2-day reduction in the mean reported number of DVD from baseline to Month 3 with a 2.6-day mean difference between OTIVIDEX and placebo in Month 3. This difference from placebo was statistically significant using a Generalize Poisson model (p=0.002). There was also a comparable reduction in vertigo frequency from baseline to Month 3 in a post hoc responder analysis with approximately 40% of patients in the OTIVIDEX groups reporting no DVDs in Month 3 (a 100% reduction from baseline).

In March 2018, we completed a Type C meeting with the FDA that included a review of the AVERTS and other clinical trial results. Based on FDA feedback, we believe that one additional successful pivotal trial is sufficient to support the U.S. registration of OTIVIDEX in Ménière's disease. We also submitted a revised statistical analysis plan for the ongoing Phase 3 clinical trial as further described below in "–Recent Developments–OTIVIDEX Program Update". We expect to complete patient enrollment in this trial, which is being conducted at approximately 60 trial sites located in Europe and the United States, in the third quarter of 2020 and announce results in the first quarter of 2021.

OTO-313 for Tinnitus

OTO-313 is a sustained-exposure formulation of gacyclidine, a potent and selective N-Methyl-D-Aspartate (NMDA) receptor antagonist, 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 tinnitus may have trouble hearing, working and sleeping. At this time, there is no cure for tinnitus and there are no FDA-approved drugs for the treatment of this debilitating condition. Based on an external market report commissioned by us, approximately 31 million, or 10%, of adults in the United States experience tinnitus with an estimated 8 million reporting moderate to severe symptoms. Approximately 1.5 million new patients are diagnosed a year. Based on an external market report commissioned by us, we believe that the total annual U.S. market opportunity for OTO-313 in tinnitus could exceed $1 billion.

Subjective tinnitus is often caused by injury to the cochlea such as by exposure to excessive noise, physical trauma, persistent ear infection or exposure to ototoxic drugs. Mechanistically, NMDA antagonists including gacyclidine may act to reduce the over-activation of auditory nerve fiber signaling that can result from cochlea injury thereby reducing the severity of the tinnitus experienced by a patient. Preclinical and previous pilot clinical data using gacyclidine support its potential as a treatment

for tinnitus. Otonomy has developed a patent-protected, sustained-exposure formulation of gacyclidine, called OTO-313, that we believe, based on animal pharmacokinetic studies, provides several weeks of drug exposure in the inner ear from a single intratympanic injection. We recently announced positive top-line results from a Phase 1/2 clinical trial for OTO-313 as further described in "–Recent Developments–Positive Top-Line OTO-313 Phase 1/2 Clinical Trial Results".

OTO-413 for Hearing Loss

OTO-413 is a proprietary, sustained-exposure formulation of brain-derived neurotrophic factor (BDNF) in development for the repair of cochlear synaptopathy, an underlying pathology in age-related and noise-induced hearing loss that manifests as speech-in-noise hearing difficulty. Cochlear synaptopathy is a condition caused by damage to ribbon synapses that has become an active focus of otology research in the last decade. Ribbon synapses are critical to hearing because they connect sound transducers in the cochlea called hair cells to auditory nerve fibers, which carry the electrical sound impulse to the brain for interpretation. Damage to ribbon synapses, for example by exposure to loud noise and/or aging, can result in hearing problems in the presence of background noise referred to as speech-in-noise hearing difficulty. This condition is estimated to affect approximately 9 million people in the United States with an even larger population having mixed hearing loss pathology that includes cochlear synaptopathy. Hearing aids provide limited benefit for speech-in-noise hearing difficulty and there is no FDA-approved drug treatment for this condition.

BDNF is a naturally occurring protein involved in neuron growth and repair. Nonclinical studies by us and other research groups have demonstrated that local administration of BDNF repairs ribbon synapses damaged due to noise trauma or exposure to ototoxic chemicals and restores hearing function. We have demonstrated proof-of-concept of OTO-413 in a preclinical model of cochlear synaptopathy and shown in animal pharmacokinetic studies that a single intratympanic injection of OTO-413 can provide several weeks of drug exposure.

We are currently enrolling patients in a Phase 1/2 clinical trial of OTO-413 for the treatment of hearing loss and recently provided an update as further described in "–Recent Developments–OTO-413 Phase 1/2 Clinical Trial Enrollment Update".

Preclinical Development Programs for Hearing Loss

Hearing loss is a large and growing problem that affects more than 360 million people worldwide and is the fourth leading cause of disability globally. Common causes include aging, noise and exposure to ototoxic drugs with genetic mutations accounting for a small but important proportion of cases. In addition to OTO-413, we have multiple development programs addressing different aspects of hearing loss that are briefly described below that afflict, by our estimates, based on an external market report commissioned by us, approximately 20 million patients in the United States.

- *GJB2 Gene Therapy Program for Congenital Hearing Loss*: We are collaborating with Applied Genetic Technologies Corporation (AGTC) to co-develop and co-commercialize an adeno-associated virus (AAV)-based gene therapy to restore hearing in patients with hearing loss caused by a mutation in the gap junction beta-2 (GJB2) gene — the most common cause of congenital hearing loss accounting for approximately 30% of cases. Patients with GJB2 mutations often have severe-to-profound hearing loss in both ears. In May 2020, we presented preclinical results at the American Society of Gene & Cell Therapy meeting demonstrating that a gene of interest can be expressed in support cells of the cochlea, which are the relevant target cells for treating GJB2 deficiency, using novel and proprietary AAV capsids and that consistent gene expression can be observed in these cells for at least 12 weeks following a single local administration. These results supported the selection of a GJB2 gene therapy candidate for further development.

- *OTO-510 Otoprotection Program*: Cisplatin and other platinum-based chemotherapeutic agents are routinely used in treating numerous tumor types with approximately 500,000 patients including 5,000 children treated each year in the United States. While use of platinum agents has contributed to improved patient survival, ototoxicity and associated permanent hearing loss is well documented in the clinical literature. In particular, cisplatin-induced hearing loss (CIHL) has been reported in more than 80% of children and young adults treated. This adversely affects speech and language development and has been associated with academic and social difficulties which can have a significant impact on patients and their families. We have identified a novel agent that potently binds to cisplatin and has demonstrated greater otoprotection than anti-oxidant and anti-apoptotic molecules, and increased potency relative to other cisplatin-binding molecules currently in development. We are conducting preclinical development for a locally-administered, sustained-exposure formulation of this agent, referred to as OTO-510, that is intended to provide otoprotection without tumor protection.
- *OTO-6XX for Severe Hearing Loss*: We have demonstrated regeneration of hair cells in a preclinical proof-of-concept model using a class of small molecules formulated for sustained-exposure local delivery, and have selected a lead compound for development. The OTO-6XX program is targeting hair cell regeneration for the treatment of severe hearing loss.

OTIPRIO, FDA-approved Treatment for Otic Infections

OTIPRIO is a single-dose, physician-administered antibacterial that was approved by the FDA in December 2015 for the treatment of pediatric patients with bilateral otitis media with effusion undergoing tympanostomy tube placement (TTP) surgery and was approved in March 2018 for the treatment of patients with acute otitis externa (AOE). OTIPRIO is the only product approved by the FDA for use during TTP surgery and is the only single-dose topical antibacterial approved for the treatment of AOE. We recently entered into a co-promotion agreement with ALK-Abelló, Inc. (ALK) to support the promotion of OTIPRIO for the treatment of AOE in physician offices in the United States.

Recent Developments

Positive Top-Line OTO-313 Phase 1/2 Clinical Trial Results

In July 2020, we announced positive top-line results from the Phase 1/2 clinical trial of OTO-313 in patients with persistent tinnitus of at least moderate severity, and our intention to advance OTO-313 into full Phase 2 development based on these results.

This study included two cohorts: the first cohort was an initial safety assessment using a lower dose of OTO-313 while the second cohort was a safety and exploratory efficacy study using a higher dose of OTO-313. Enrollment criteria for the second cohort included unilateral, persistent tinnitus of cochlear origin, less than six months from onset. For enrollment, patients had to report at least moderate tinnitus severity at baseline, achieving a Tinnitus Functional Index (TFI) score, a clinically validated instrument, greater or equal to 25.

The exploratory efficacy cohort of the Phase 1/2 clinical trial included a total of 35 patients of which 31 were evaluable (4 patients withdrew from the study unrelated to adverse events). The evaluable patients were randomized to receive a single intratympanic injection of OTO-313 or placebo (1:1 randomization) and then followed for eight weeks. In addition to completing the TFI instrument at regular intervals, patients reported their tinnitus loudness and annoyance using a daily phone diary and also completed the Patient Global Impression of Change (PGIC). The study achieved its objectives by demonstrating a positive clinical signal for OTO-313 based on a TFI responder analysis, with an acceptable safety profile.

Top-line results for the Phase 1/2 clinical trial are as follows:

- 43% of OTO-313 patients were responders at both Day 29 and Day 57 compared to 13% of placebo patients. A responder is a patient whose TFI score decreases by 13-points or more from their baseline score, a change considered clinically meaningful based on the TFI instrument validation.
- For patients who were responders at both Day 29 and Day 57, OTO-313 demonstrated a higher responder rate than placebo at all TFI improvement levels considered clinically meaningful (TFI reduction ≥ 13, 15, 20, 25, and 30 points). The difference in responder rate between OTO-313 and placebo was statistically significant on post hoc analysis (p value < 0.05) for TFI reductions ≥ 13, 15, and 20 points.
- OTO-313 patients who were responders at both Day 29 and Day 57 reported improvements in both tinnitus loudness and annoyance levels based on daily diaries and also reported improvement in the PGIC, a general assessment of tinnitus status. There was a very strong relationship demonstrated between the improvement in TFI score reported by these OTO-313 responders and their improvement in tinnitus loudness and annoyance levels as well as PGIC based on the calculated correlation coefficients of ≥ 0.8 for these endpoints.
- A single intratympanic injection of OTO-313 was well-tolerated with lower incidence of adverse events than the placebo group.

Given these results, we intend to advance OTO-313 into full Phase 2 development which may include evaluation of a higher dose and/or retreatment with OTO-313.

OTIVIDEX Program Update

In July 2020, we provided an update on the statistical analysis plan for the ongoing OTIVIDEX Phase 3 clinical trial in Ménière's disease. In response to questions received from the U.S. Food and Drug Administration (FDA) regarding use of the Generalized Poisson model to analyze the daily vertigo count data reported by patients, we submitted a revised statistical analysis plan that uses a statistical test called the Negative Binomial model for the primary analysis of the ongoing trial.

We selected the Negative Binomial model to address the FDA's questions because we believe it provides the best fit of the OTIVIDEX clinical data based on the Phase 2b trial (for patients with vertigo enrollment criteria matching the Phase 3 clinical trials), the AVERTS-2 Phase 3 clinical trial, and the integrated dataset from both trials. As the table below indicates, the ad hoc analysis of the Definitive Vertigo Day (DVD) count data reported by patients for Month 3 is statistically significant (p value < 0.05) using the Negative Binomial model for each of these prior trial populations as well as the integrated summary.

p value for Analysis of DVD Count in Month 3	Phase 2b* (n = 97)	AVERTS-2** (n = 111)	Integrated Dataset
Generalized Poisson Model	0.002	0.013	< 0.001
Negative Binomial Model	0.016	0.008	< 0.001

* Patients with baseline DVD count of 4-22 days during the one-month baseline period
** Patients who completed 3-month follow-up period (of which 105 completed daily diaries)

Based on the increased power of the Negative Binomial model to detect a treatment benefit compared to the Generalized Poisson model, we are revising our target enrollment for the ongoing Phase 3 clinical trial to approximately 142 patients. We believe that this smaller target enrollment size will still provide greater than 90% power to detect a statistically significant treatment benefit with p value < 0.05.

OTO-413 Phase 1/2 Clinical Trial Enrollment Update

In June 2020, we reported that we had successfully escalated through three dose levels totaling 24 patients for our Phase 1/2 clinical trial. This trial is a single ascending dose study expected to enroll approximately 40 patients with speech-in-noise hearing difficulty and normal up to moderately-severe hearing loss by conventional testing. We have initiated enrollment for the high dose cohort, for which we expect to enroll approximately 16 patients in this cohort, randomized 3:1 for a single intratympanic injection of OTO-413 or placebo. Following treatment, patients undergo repeated testing for safety and exploratory efficacy over three months. Results are expected for this trial in the fourth quarter of 2020.

OTIPRIO Co-Promotion Agreement

In June 2020, we entered into a co-promotion agreement that provides ALK with an exclusive right to promote OTIPRIO for AOE to office-based health care professionals in the United States including ear, nose and throat (ENT) physicians, pediatricians and primary care physicians. During the multi-year agreement, we will receive co-promotion fees and reimbursement of a proportion of product support costs while also retaining a share of adjusted gross profits from the sale of OTIPRIO for use in AOE.

COVID-19

Given the unprecedented and evolving nature of the COVID-19 pandemic, there continues to be significant uncertainty about the progression and ultimate impact of the pandemic on our business operations. We have taken steps to mitigate the impact of the COVID-19 pandemic on our clinical trials, including developing processes to ensure the integrity of data collection from enrolled patients and supporting the increasing number of sites able to enroll new patients, among other activity. Nonetheless, we do not know the full extent of potential future delays or impacts on our business operations, our preclinical programs and clinical trials, healthcare systems, our financial condition, or the global economy as a whole resulting from the COVID-19 pandemic.

In addition, as a result of the COVID-19 pandemic, we have taken steps to protect the health and safety of our employees and community by generally adopting a work from home policy in line with directives from the State of California and the applicable local governments, and guidance from the U.S. Centers for Disease Control and Prevention (CDC). On-site activities have been restricted to certain essential facility and laboratory support functions and various safety protocols have been implemented.

Corporate Information

We were incorporated in the state of Delaware on May 6, 2008. Our principal executive offices are located at 4796 Executive Drive, San Diego, California 92121, and our telephone number is (619) 323-2200. 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 supplement or the accompanying prospectus, and you should not consider information on our website to be part of this prospectus supplement or the accompanying prospectus.

Otonomy, the Otonomy logo, OTIPRIO, OTIVIDEX and other trademarks or service marks of Otonomy appearing in this prospectus supplement and the accompanying prospectus are the property of Otonomy. This prospectus supplement and the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and in the prospectus contain additional trade names, trademarks and service marks of other companies. We do not intend our use or display of other companies' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies. We have omitted the ® and ™ designations, as applicable, for the trademarks used in this prospectus supplement.

THE OFFERING	
Common stock offered by us	14,500,000 shares
Pre-funded warrants offered by us	We are also offering, in lieu of common stock to certain investors that so choose, pre-funded warrants to purchase 4,000,000 shares of our common stock. The purchase price of each pre-funded warrant equals the price per share at which shares of common stock are being sold to the public in this offering, minus $0.001, and the exercise price of each pre-funded warrant equals $0.001 per share. Each pre-funded warrant will be exercisable from the date of issuance until the date the warrant is exercised in full, subject to an ownership limitation. See “Description of Pre-Funded Warrants.” This prospectus supplement also relates to the offering of the shares of common stock issuable upon the exercise of such pre-funded warrants.
Option to purchase additional shares	We have granted the underwriters an option, exercisable for 30 days after the date of this prospectus supplement, to purchase up to an additional 2,775,000 shares from us.
Common stock to be outstanding after this offering	45,314,211 shares (or 48,089,211 shares if the underwriters exercise their option to purchase additional shares in full).
Use of proceeds	We estimate that the net proceeds from this offering, after deducting underwriting discounts and commissions and estimated offering expenses, will be approximately $55.8 million (or approximately $64.2 million if the underwriters exercise their option to purchase additional shares in full). We currently intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and short-term investments, to fund the development of OTIVIDEX; the Phase 2 clinical development program for OTO-313; the development of OTO-413; further advancement of our other programs including our GJB2 gene therapy program; and the remainder for other research and development activities, working capital, and other general corporate purposes. See “Use of Proceeds.”

Risk factors	You should read the “Risk Factors” section of this prospectus supplement and in the documents incorporated by reference in this prospectus supplement and accompanying prospectus for a discussion of factors to consider before deciding to purchase shares of our common stock or pre-funded warrants.
Nasdaq Global Select Market symbol	Our common stock is listed on The Nasdaq Global Select Market under the symbol “OTIC.” There is no established public trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on The Nasdaq Global Select Market or any other national securities exchange or nationally recognized trading system. Without an active trading market, the liquidity of the pre-funded warrants will be limited. See “Description of Pre-Funded Warrants”.

The number of shares of common stock to be outstanding following this offering is based on 30,814,211 shares of our common stock outstanding as of March 31, 2020, and excludes:

- 10,052,847 shares of our common stock issuable upon the exercise of options outstanding as of March 31, 2020, with a weighted-average exercise price of $4.19 per share;
- 2,531,206 shares of our common stock reserved for future issuance as of March 31, 2020 under our 2014 Equity Incentive Plan;
- 2,439,428 shares of our common stock reserved for issuance as of March 31, 2020 under our employee stock purchase plan;
- shares of our common stock that may be sold from time to time under an “at the market” equity offering program that we entered into on August 1, 2019 with Cowen and Company, LLC, of which no shares have been sold to date; and
- pre-funded warrants to purchase up to 4,000,000 shares of our common stock at an exercise price of $0.001 per share.

Unless otherwise indicated, all information in this prospectus supplement assumes no exercise of outstanding options, no grants of awards, no purchase and exercise of pre-funded warrants by any purchaser in this offering and no exercise by the underwriters of their option to purchase additional shares of common stock in this offering.

RISK FACTORS

An investment in our securities involves a high degree of risk. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed below and discussed under the section entitled "Risk Factors" contained in our Annual Report on Form 10-K for the fiscal year ended December 31, 2019 and our Quarterly Report on Form 10-Q for the quarter ended March 31, 2020, as updated by our subsequent filings under the Securities Exchange Act of 1934, as amended (the Exchange Act), each of which is incorporated by reference in this prospectus supplement and accompanying prospectus in their entirety, together with all of the other information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein and therein, and any related free writing prospectus. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations. The occurrence of any of these known or unknown risks might cause you to lose all or part of your investment in the offered securities.

Risks Related to Our Financial Condition and Capital Requirements

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

We are a commercial-stage biopharmaceutical company with a limited operating history upon which you can evaluate our business and prospects. We are not profitable and have incurred losses in each year since we commenced operations in 2008. In addition, we have limited experience and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical industry. Drug development is a highly speculative undertaking and involves a substantial degree of risk. To date, we have obtained U.S. regulatory approval and launched a single product, OTIPRIO, but have not yet generated significant revenue. We continue to incur significant research and development expenses related to our clinical trials and product development activities and other selling, general and administrative expenses. We have recorded net losses of $11.8 million and $12.0 million for the three months ended March 31, 2020 and 2019, respectively. As of March 31, 2020, we had an accumulated deficit of $471.7 million.

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

We expect to continue to incur significant losses for the foreseeable future. Our ability to achieve significant revenue and profitability is dependent on our ability to complete the development of our product candidates, obtain necessary regulatory approvals and successfully commercialize our products. We may never succeed in these activities and may never generate revenue that is significant or large enough to achieve profitability. We launched OTIPRIO in March 2016, but we have not generated significant revenue from sales of OTIPRIO, and in November 2017, we announced the discontinuation of our promotional support for OTIPRIO in TTP surgery. In August 2018, we announced the initiation of a partnership with Mission, and in May 2019, we announced the initiation of a partnership with Glenmark, both for the promotion of OTIPRIO to certain end users involved in the treatment of patients for AOE. In July 2019, we were notified by Glenmark of its early discontinuation of OTIPRIO promotional support activities due to the delay in FDA approval of its Ryaltris allergy product, and the impact of such delay on its business operations. In August 2019, Mission informed us of its non-renewal of the co-promotion agreement.

We recently entered into a co-promotion agreement with ALK-Abelló, Inc. (ALK) to support the promotion of OTIPRIO for the treatment of AOE in physician offices in the United States but there are

no assurances that such partnership will be successful or that it will not be terminated earlier than we expect. We may also seek other promotional partners for OTIPRIO, but there are no assurances that we can find a new promotional partner or that the terms and timing of any such arrangements would be acceptable to us. Such partnerships may not generate significant revenue, may not be successful, and may be terminated. In addition, we currently have limited sales and marketing capabilities. If we are unable to enter into arrangements on acceptable terms or at all, or if such arrangements are not successful, we may not be able to successfully commercialize our products or generate product revenue. Any failure or delay in entering promotional partnerships or developing our internal sales, marketing and distribution capabilities could adversely impact the commercialization of our products. If we are not successful in commercializing our products, either on our own or through partnering with one or more third parties, our future product revenue may suffer and we could incur significant additional losses. Even if we achieve profitability in the future, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital and any failure to become and remain profitable may adversely affect the market price of our common stock, our ability to raise capital, and our viability.

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

Since our inception, most of our resources have been dedicated to the development of OTIPRIO and our product candidates, OTIVIDEX, OTO-311 (now OTO-313) and OTO-413. In particular, conducting clinical trials for OTIVIDEX, OTO-313 and OTO-413 will require substantial funds. We have previously funded our operations primarily through the sale and issuance of common stock, convertible preferred stock and convertible notes. Our existing cash, cash equivalents and short-term investments are not sufficient to fund our operations for a period of at least twelve months from the date of this prospectus supplement and as a result we believe there is substantial doubt with respect to our ability to continue as a going concern. However, we believe that our existing cash, cash equivalents and short-term investments together with net proceeds of this proposed offering will be sufficient to fund our operations for at least twelve months from the date of this prospectus supplement.

We believe that we will continue to expend substantial resources for the foreseeable future for the continued development of OTIVIDEX, OTO-313, OTO-413 and any other product candidates we may choose to pursue. These expenditures will include costs associated with marketing and selling any products approved for sale, manufacturing, preparing regulatory submissions, and conducting nonclinical studies and clinical trials. We cannot estimate with reasonable certainty the actual amounts necessary to successfully complete the development and commercialization of our product candidates.

Our future capital requirements depend on many factors, including:

- the timing of, and the costs involved in, nonclinical and clinical development and obtaining regulatory approvals for OTIVIDEX, OTO-313, OTO-413 or any other product candidates;
- the cost of manufacturing OTIPRIO and our product candidates;
- the revenue generated by OTIPRIO and our product candidates, if approved;
- the cost of commercialization activities for OTIPRIO and any of our product candidates that may be approved for sale, if any, including marketing, sales and distribution costs;
- the number and characteristics of any other product candidates we develop or acquire;
- our ability to establish and maintain strategic collaborations, licensing, development or commercialization arrangements and the terms and timing of such arrangements, including whether we are able to timely find a new promotional partner for OTIPRIO;

- the degree and rate of market acceptance of OTIPRIO and any other approved products;
- the emergence, approval, availability, perceived advantages, relative cost, relative safety and relative efficacy of other products or treatments;
- the expenses needed to attract and retain skilled personnel;
- the costs associated with being a public company;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims and other intellectual property rights, including litigation costs and the outcome of such litigation;
- the extent to which we are required to pay milestone or other payments under our in-license agreements and the timing of such payments; and
- the cost of litigation, including any product liability or other lawsuits related to our products.

Additional capital may not be available when we need it, on terms that are acceptable to us or at all. In addition, our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and the recent disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the COVID-19 pandemic. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate our sales and marketing, manufacturing or distribution capabilities or other activities that may be necessary to commercialize our product or product candidates, nonclinical studies, clinical trials or other development activities.

If we raise additional capital through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish certain valuable rights to our product or product candidates, technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable to us. In addition, we have a sales agreement in place with Cowen and Company, LLC to sell up to $40.0 million worth of shares of our common stock, from time to time, through an “at the market” equity offering program under which Cowen and Company, LLC will act as sales agent or principal. As of March 31, 2020, $40.0 million worth of shares of our common stock remained available for sale under the “at the market” equity offering program. If we raise additional capital through our “at the market” equity offering program, or other public or private equity offerings, the ownership interest of our existing stockholders will be diluted and the terms of any new equity securities may have preferential rights over our common stock. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt or making capital expenditures or specified financial ratios, any of which could restrict our ability to commercialize our product, develop and commercialize our product candidates or operate as a business. Any collaboration agreements we enter into may provide capital in the near-term but limit our potential cash flow and revenue in the future. Any of the foregoing could significantly harm our business, financial condition and prospects.

A pandemic, epidemic or outbreak of an infectious disease, such as COVID-19, or the perception of its effects, could materially and adversely affect our business, operations and financial condition.

Outbreaks of epidemic, pandemic or contagious diseases, such as COVID-19, could significantly disrupt our business. Such outbreaks pose the risk that we or our employees, contractors, suppliers, and other partners may be prevented from conducting business activities for an indefinite period of time due to spread of the disease, or due to shutdowns that may be requested or mandated by federal, state and local governmental authorities. Business disruptions could include disruptions or restrictions on our ability to travel, as well as temporary closures of our facility, the facilities of our partners, clinical trial sites, service providers, suppliers or contract manufacturers. While it is not possible at this time to

estimate the overall impact that the COVID-19 pandemic could have on our business, the continued rapid spread of COVID-19, both across the United States and through much of the world, and the measures taken by the governments of countries and local authorities affected has disrupted and could delay our ongoing clinical trials, and could disrupt and delay our preclinical activities, the manufacture or shipment of both drug substance and finished drug product for preclinical testing and clinical trials and adversely impact our business, financial condition or operating results.

For example, the state of California, where our corporate offices are located, has issued orders for all residents to remain at home, except as needed for essential activities as a result of the COVID-19 pandemic and we have had to implement work from home policies that may continue for an indefinite period. We have taken steps to protect the health and safety of our employees and community, while working to ensure the sustainability of our business operations as this unprecedented situation continues to evolve. We continue to evaluate the impact COVID-19 may have on our ability to effectively conduct our business operations as planned, and work with healthcare providers supporting our clinical studies to mitigate risk to patients while taking into account regulatory, institutional, and government guidance and policies, but there can be no assurance that we will be able to avoid part or all of any impact from the spread of COVID-19 or its consequences.

We have clinical trial sites in the United States and Europe, which may be affected by travel or quarantine restrictions imposed by federal, state or local governments due to the COVID-19 pandemic. The enrollment of new patients in our OTIVIDEX trial is being managed on a site-by-site basis according to local conditions. We temporarily paused new patient enrollment in our Phase 1/2 clinical trial of OTO-413 but have resumed enrollment on a site-by-site basis. In light of the significant uncertainty regarding the impact of the COVID-19 pandemic, we had suspended and subsequently updated our guidance regarding timing of trial results. We may in the future need to further update or suspend such guidance as a result of the impact of the COVID-19 pandemic. In addition, we have made and we (and our contract research organizations (CROs)) may need to make certain adjustments to the operation of clinical trials in an effort to ensure the monitoring and safety of patients and minimize risks to trial data integrity during the pandemic in accordance with the guidance issued by the FDA in March 2020 and updated in April 2020.

Third-party manufacturers which we use for the supply of materials for our product candidates or other materials necessary to conduct preclinical studies and clinical trials are located in countries affected by COVID-19. Although we expect no material impact on the clinical supply of our product candidates for our current clinical trials, should our third-party manufacturers experience extended disruptions, we could experience delays in future trials.

Furthermore, the spread of the virus may affect the operations of key governmental agencies, such as the FDA and similar organizations outside the United States, as well as local regulatory agencies and health officials, which may delay the development of our product candidates.

The COVID-19 pandemic continues to rapidly evolve. The extent to which COVID-19 impacts our business will depend on future developments, which are highly uncertain and cannot be predicted, such as the ultimate geographic spread of the disease, the duration of the pandemic, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease and to address its impact, including on financial markets or otherwise. While the extent of the impact of the COVID-19 pandemic on our business and financial results is uncertain, a continued and prolonged public health crisis could have a material negative impact on our business, financial condition and operating results.

Risks Related to Our Product and Product Candidates

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

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

OTIVIDEX is subject to the risks associated with completing such pivotal trial and any future clinical trials required for registration, including risks associated with:

- the successful and timely implementation, enrollment and completion of such clinical trials of OTIVIDEX;
- the potential impacts of the COVID-19 pandemic;
- the use and adequacy of patient reported outcomes in such clinical trials;
- our ability to demonstrate with substantial clinical evidence the safety and efficacy of OTIVIDEX in such clinical trials;
- the successful implementation and completion of any additional clinical safety studies or any additional non-clinical studies that may be required by the FDA; and
- the ability to submit a New Drug Application (NDA) for regulatory approval to the FDA.

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

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

Many of these clinical, regulatory and commercial matters are beyond our control and are subject to other risks described elsewhere in this "Risk Factors" section. Accordingly, we cannot assure you

that we will be able to advance OTIVIDEX through final clinical development, or obtain regulatory approval of, manufacture, commercialize or generate significant revenue from OTIVIDEX. If we cannot do so, or are significantly delayed in doing so, our business will be materially harmed.

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

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

- generating sufficient data to support the initiation or continuation of clinical trials;
- obtaining regulatory approval to commence clinical trials;
- contracting with the necessary parties to conduct clinical trials;
- enrolling sufficient numbers of subjects or patients in clinical trials;
- the use and adequacy of patient reported outcomes in such clinical trials;
- our ability to demonstrate with substantial clinical evidence the safety and efficacy of such product candidates in such clinical trials;
- the timely manufacture of sufficient quantities of the product candidate for use in clinical trials; and
- adverse events in the clinical trials.

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

Risks Related to Our Business and Strategy

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

OTIPRIO and our product candidates, if approved, may not achieve market acceptance among physicians and patients, and may not be commercially successful. For OTIPRIO, treatment of pediatric patients with bilateral otitis media with effusion undergoing TTP surgery is currently addressed with the off-label use of antibiotic ear drops, but antibiotic ear drops are approved for the AOE indication. We launched OTIPRIO in March 2016, but we have not generated significant revenue from sales of OTIPRIO, and in November 2017, we announced the discontinuation of our promotional support for OTIPRIO in TTP surgery. In August 2018, we announced the initiation of a partnership with Mission, and in May 2019, we announced the initiation of a partnership with Glenmark, both for the promotion of OTIPRIO to certain end users involved in the treatment of patients for AOE. In July 2019, we were notified by Glenmark of its early discontinuation of OTIPRIO promotional support activities due to the delay in FDA approval of its Ryaltris allergy product, and the impact of such delay on its business operations. In August 2019, Mission informed us of its non-renewal of the co-promotion agreement. We

recently entered into a co-promotion agreement with ALK to support the promotion of OTIPRIO for the treatment of AOE in physician offices in the United States but there are no assurances that such partnership will be successful or that it will not be terminated earlier than we expect.

There are currently no FDA-approved drug treatments for the indications we are pursuing for our product candidates. Our proposed initial indication for OTIVIDEX is the treatment of vertigo associated with Ménière's disease. Currently, Ménière's disease patients are routinely prescribed a low-salt diet and off-label use of diuretics. Physicians may also prescribe the off-label use of antihistamines, anticholinergics, phenothiazines and benzodiazepines as well as corticosteroids. Our proposed indication for OTO-313 is the treatment of tinnitus. Currently, physicians may attempt to treat tinnitus symptoms with the off-label use of steroids, anxiolytics, antidepressants, and antipsychotics. Our target indication for OTO-413 is the treatment of speech-in-noise hearing difficulties. A subset of patients with this condition are currently treated with hearing aids. The commercial success of OTIPRIO and our product candidates, if approved, will depend significantly on the adoption and use of the resulting products by physicians for approved indications. The decision to elect treatment with OTIPRIO for middle ear effusion in pediatric patients requiring TTP surgery and AOE, or to elect to utilize OTIVIDEX for Ménière's disease, OTO-313 for tinnitus or OTO-413 for speech-in-noise hearing difficulties, rather than other products or treatments, may be influenced by a number of factors, including:

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

Our assessment of the potential market opportunity for our product candidates is based on industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties, some of which we commissioned. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such

information. While we believe these industry publications and third-party research, surveys and studies are reliable, we have not independently verified such data. Similarly, although the studies we have commissioned are based on information that we believe to be complete and reliable, we cannot guarantee that such information is accurate or complete. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research and other surveys, which may be based on a small sample size and fail to accurately reflect market opportunities. Further, we have commissioned a number of market studies that are specific to us and to our product candidates and used the results of these studies to help assess our market opportunity. While we believe that our internal assumptions and the bases of our commissioned studies are reasonable, no independent source has verified such assumptions or bases. If any of our assumptions or estimates, or these publications, research, surveys or studies prove to be inaccurate, then the actual market for our product candidates may be smaller than we expect, and as a result our product revenue may be limited and it may be more difficult for us to achieve or maintain profitability.

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

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

Clinical testing is expensive, can take many years to complete and its outcome is inherently uncertain. A failure of one or more of our clinical trials can occur at any time during the clinical trial process. The results of nonclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. There is a high failure rate for drugs proceeding through clinical trials, and product candidates in later stages of clinical trials may fail to show the required safety and efficacy despite having progressed through nonclinical studies and initial clinical trials. For instance, our AVERTS-2 Phase 3 clinical trial for OTIVIDEX in Ménière's disease patients, conducted in Europe, achieved its primary endpoint, while our AVERTS-1 Phase 3 clinical trial, conducted in the United States, did not. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier clinical trials, and we cannot be certain that we will not face similar setbacks. Even if our clinical trials are completed, the results may not be sufficient to obtain regulatory approval for our product candidates or support the indications which we are pursuing.

From time to time, we may publicly disclose preliminary, interim or top-line data from our clinical trials. These interim updates are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, top-line data should be viewed with caution until the final data are available. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between interim data and final data could

materially affect our business, financial condition, results of operations and growth prospects. If the preliminary or top-line data that we report differ from late, final or actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize our product candidates may be harmed, which could materially affect our business, financial condition, results of operations and growth prospects.

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

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

Patient enrollment is a significant factor in the timing of clinical trials. We may not be able to initiate or continue clinical trials for our product candidates on a timely basis if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials. Patient enrollment is affected by many factors, including the size and nature of the patient population, the proximity of and access by patients to clinical sites, the eligibility criteria for the clinical trial, the design of the clinical trial, competing clinical trials, 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, and factors, including quarantine restrictions, due to the COVID-19 pandemic.

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

For example, OTIVIDEX was previously subject to Full Clinical Hold that was removed in July 2013 and then subject to Partial Clinical Hold that was removed in June 2014. The removal of Full Clinical

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

We received questions from the FDA regarding use of the Generalized Poisson model to analyze the daily vertigo count data reported by patients in our ongoing OTIVIDEX Phase 3 clinical trial, and we have submitted to the FDA a revised statistical analysis plan that uses a statistical test called the Negative Binomial model for the primary analysis of this ongoing trial. We cannot guarantee that the FDA will agree with this approach, and if not, this could cause future delays. Additionally, we cannot guarantee that our revised statistical analysis plan and associated target enrollment plan will be adequate.

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

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

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

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

- our inability to satisfactorily demonstrate that the product candidates are safe and effective for the requested indication;
- the FDA's disagreement with our trial protocol or the interpretation and analysis of data from nonclinical studies or clinical trials;
- the population studied in the clinical trial may not be sufficiently broad or representative to assess safety in the full population for which we seek approval;
- our inability to demonstrate that clinical or other benefits of our product candidates outweigh any safety or other perceived risks;
- the FDA's determination that additional nonclinical or clinical trials are required;
- the FDA's non-approval of the formulation, labeling or the specifications of our product candidates;

- the FDA's failure to accept the manufacturing processes or facilities of third-party manufacturers with which we contract, or our inability to manufacture our product candidates pursuant to cGMP; or
- the potential for approval policies or regulations of the FDA to significantly change in a manner rendering our clinical data insufficient for approval.

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

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

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

Some patients in our clinical trials have reported adverse events after being treated with OTIPRIO, OTIVIDEX and OTO-313. For example, in the Phase 1/2 clinical trial for OTO-313, one patient reported symptoms associated with Grade 2 (moderate) stress cardiomyopathy, a serious adverse event, which was determined not to be treatment related, and four other patients reported Grade 1 (mild) or Grade 2 (moderate) adverse events. If we are successful in commercializing our product or product candidates, the FDA and other foreign regulatory agency regulations will require that we promptly report certain information about adverse medical events if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We may fail to report adverse events we become aware of within the prescribed timeframe. We may also fail to appreciate that we have become aware of a reportable adverse event, especially if it is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of our product or product candidates. If we fail to comply with our reporting obligations, the FDA or other foreign regulatory agencies could take action including criminal prosecution, the imposition of civil monetary penalties, seizure of our products, or delay in approval or clearance of future products.

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

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

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

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

We and the third parties upon whom we rely are required to comply with GCP, which are regulations and guidelines enforced by regulatory authorities around the world for products in clinical development. Regulatory authorities enforce these GCP regulations through periodic inspections of clinical trial sponsors, principal investigators and clinical trial sites. If we or our third parties fail to

comply with applicable GCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and our submission of marketing applications may be delayed, or the regulatory authorities may require us to perform additional clinical trials before reviewing or approving our marketing applications. We cannot assure you that, upon inspection, a regulatory authority will determine that any of our clinical trials comply or complied with applicable GCP regulations.

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

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

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

Reliance on third-party manufacturers entails additional risks, including reliance on the third party for regulatory compliance and quality assurance (including compliance with cGMPs), the possible

breach of the manufacturing agreement by the third party, and the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us. The facilities used by our third-party manufacturers must be accepted by the FDA pursuant to inspections that will be conducted before approval and after we submit our NDA to the FDA. We do not control the implementation of the manufacturing process of, and are completely dependent on, our third-party manufacturers for compliance with the regulatory requirements, for manufacture of both active drug substances and finished drug products. If our third-party manufacturers cannot successfully manufacture material that conforms to applicable specifications in our regulatory applications and the strict regulatory requirements of the FDA or foreign regulatory authorities, we will not be able to secure and/or maintain regulatory acceptance of our contract manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers or other third-party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. The failure of our third-party manufacturers to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of OTIPRIO or our product candidates or any other product candidates or products that we may develop. In addition, if the FDA does not accept these facilities for the manufacture of our product or our product candidates or if it withdraws any such acceptance in the future, we will need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Any failure or refusal to supply the components for our product or our product candidates could delay, prevent or impair our clinical development or commercialization efforts. If our contract manufacturers were to breach or terminate their manufacturing arrangements with us, the development or commercialization of the affected product or product candidates could be delayed, which could have an adverse effect on our business. Any change in our manufacturers could be costly because the commercial terms of any new arrangement could be less favorable and because the expenses relating to the transfer of necessary technology and processes could be significant.

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

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

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

We depend on the availability of key raw materials, including poloxamer for OTIPRIO and our product candidates, ciprofloxacin for OTIPRIO, dexamethasone for OTIVIDEX, gacyclidine for OTO-313 and BDNF for OTO-413, from a small number of third-party suppliers. Because there are a limited number of suppliers for the raw materials that we use to manufacture our product and product

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

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

OTIPRIO is currently approved for the treatment of pediatric patients with bilateral otitis media with effusion undergoing TTP surgery and for the treatment of AOE and is in development for acute otitis media with tubes. We are developing OTIVIDEX for the treatment of vertigo associated with Ménière's disease, OTO-313 for the treatment of tinnitus and OTO-413 for the treatment of speech-in-noise hearing difficulties. The FDA and other applicable regulatory agencies will restrict our ability to market and advertise our products to the scope of the approved label for the applicable product and for no other indications, which could limit physician and patient adoption. We may attempt to develop new treatment indications for our product or product candidates in the future, but we cannot predict when or if we will receive the regulatory approvals required to promote our product or product candidates for new treatment indications. Failure to receive such approvals prevents us from promoting and commercializing the new treatment indications. In addition, we would be required to conduct additional clinical trials or studies to support approvals for additional indications, which would be time consuming and expensive, and may produce results that do not support regulatory approvals. If we do not obtain additional regulatory approvals, our ability to expand our business will be limited.

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

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

on the sale or marketing of our products or significant fines and penalties, and the imposition of these sanctions could also affect our reputation with physicians, patients and caregivers, and our position within the industry.

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

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

We have limited experience in the marketing and sale of pharmaceutical products, and there are significant risks involved in managing a sales and marketing organization, including our ability to hire, retain, adequately compensate and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel and effectively manage a geographically dispersed sales and marketing team. For example, we discontinued promotional support for OTIPRIO and, as a result, no longer have a sales force. If we decide not to promote our product candidates ourselves, if approved, we may consider promotional partnership arrangements. For instance, in August 2018, we announced the initiation of a partnership with Mission, and in May 2019, we announced the initiation of a partnership with Glenmark, both for the promotion of OTIPRIO to certain end users involved in the treatment of patients for AOE. In July 2019, we were notified by Glenmark of its early discontinuation of OTIPRIO promotional support activities due to the delay in FDA approval of its Ryaltris allergy product, and the impact of such delay on its business operations. In August 2019, Mission informed us of its non-renewal of the co-promotion agreement.

We recently entered into a co-promotion agreement with ALK to support the promotion of OTIPRIO for the treatment of AOE in physician offices in the United States but there are no assurances that such partnership will be successful or that it will not be terminated earlier than we expect. We may also seek other promotional partners for OTIPRIO, but there are no assurances that we can find a new promotional partner or that the terms and timing of any such arrangements would be acceptable to us. Such partnerships may not generate significant revenue, may not be successful, and may be terminated. If we are unable to enter into such arrangements on acceptable terms or at all, or if such arrangements are not successful, we may not be able to successfully commercialize our products or generate product revenue. Any failure or delay in entering promotional partnerships or developing our internal sales, marketing and distribution capabilities would adversely impact the commercialization of our products. If we are not successful in commercializing our products, either on our own or through partnering with one or more third parties, our future product revenue will suffer and we would incur significant additional losses.

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

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

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

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

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

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

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

Obtaining coverage and reimbursement approval for a product from a government or other third-party payor is a time consuming and costly process that could require us to provide supporting

scientific, clinical and cost-effectiveness data for the use of our products to the payor. There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the medicine is approved by the FDA or other comparable foreign regulatory authorities. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement or to have pricing set at a satisfactory level. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels such as may result where alternative or generic treatments are available, we may be unable to achieve or sustain profitability.

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

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

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

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

In March 2010, the Affordable Care Act (ACA) became law in the United States. One goal of ACA is to reduce the cost of healthcare and substantially change the way healthcare is financed by both governmental and private insurers. While we cannot fully predict what impact on federal reimbursement policies this legislation will continue to have in general or on our business specifically,

ACA may result in downward pressure on pharmaceutical reimbursement, which could negatively affect our ability to generate revenue, achieve market acceptance of our product or future approved products, attain profitability, or commercialize our product or any future approved products. Provisions of ACA relevant to the pharmaceutical industry include the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, not including orphan drug sales;
- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% (increased pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) 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, 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 the ACA and its implementing regulations, including reporting any payment or "transfer of value" provided to physicians, as defined by such law, and teaching hospitals and any ownership and investment interests held by physicians and their immediate family members during the preceding calendar year (effective January 1, 2022, these reporting obligations will extend to include payments and transfers of value made during the previous year to certain non-physician providers such as physician assistants and nurse practitioners);
- 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.

There have been judicial and Congressional challenges to certain aspects of the ACA, as well as efforts by the Trump administration to repeal or replace certain aspects of the ACA and we expect such challenges and amendments to continue. The U.S. Supreme Court is expected to review the constitutionality of the ACA in the fall following a series of federal cases that began with a district court ruling that the ACA is unconstitutional in its entirety because the "individual mandate" provisions of the ACA were repealed by Congress. The U.S. government could repeal or change some or all of the ACA, and complying with any new legislation or reversing changes implemented under the ACA could be time-intensive and expensive, resulting in a material adverse effect on our business. Until the ACA or other healthcare reform measures are fully implemented or there is more certainty concerning the future of the ACA or such healthcare reform measures, it will be difficult to predict its full impact and influence on our business. Healthcare reform measures that may be adopted in the future may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for our product

or future approved products. Any such reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, achieve market acceptance of our product or future approved products, attain profitability, or commercialize future approved products.

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

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

- decreased demand for our products;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants or cancellation of clinical trials;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to clinical trial participants or patients;
- regulatory investigations, product recalls, withdrawals or labeling, marketing or promotional restrictions;
- exhaustion of any available insurance and our capital resources;
- loss of revenue; and
- the inability to commercialize any products we develop.

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

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

Our success depends, in part, on our continued ability to attract, retain and motivate highly qualified management, commercial, clinical and scientific personnel. We believe that our future

success is highly dependent upon the contributions of our senior management, particularly our President and Chief Executive Officer, as well as our senior scientists and other members of our senior management team. The loss of services of any of these individuals, who all have at-will employment arrangements with us, could delay or prevent the successful development of our product pipeline, completion of our planned clinical trials or the commercialization of our product candidates, if approved.

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

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

Although a substantial amount of our efforts are focused on the development and regulatory approval of our current product candidates, a key element of our strategy is to identify, develop and commercialize additional product candidates for the treatment of neurotology 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, or our partners, may fail or suffer security breaches, which could result in a material disruption of our drug development programs.

We rely on information technology systems to keep financial records, maintain laboratory and corporate records, communicate with staff and external parties, collect, store and transmit large amounts of confidential information (including intellectual property, proprietary business information and personal information), and operate other critical functions. Despite the implementation of security measures, our internal computer systems and those of our third-party logistics vendors, CROs and other contractors and consultants, and our partners, are vulnerable to damage from computer viruses, unauthorized access or use resulting from malware, denial-of-service attacks, cyber-attacks or cyber-intrusions over the Internet, hacking, phishing and other social engineering attacks, natural disasters, terrorism, war and telecommunication and electrical failures. To our knowledge, we have not experienced a material system failure, accident or security breach to date, and if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our commercialization activities or drug development programs. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach (whether to our systems or to our CROs or other contractors, consultants, or partners) were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential, proprietary, or other protected information, we could incur liability and penalties and the development and commercialization of our product candidates could be delayed.

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

Generally accepted accounting principles in the United States are subject to interpretation by the Financial Accounting Standards Board, the SEC and various bodies formed to promulgate and

interpret appropriate accounting principles. A change in accounting standards or practices can have a significant effect on our reported results and may even affect our reporting of transactions completed before the change is effective. New accounting pronouncements and varying interpretations of accounting pronouncements have occurred and may occur in the future. Changes to existing rules or the questioning of current practices may adversely affect our reported financial results or the way we conduct our business.

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

We are exposed to the risk that our employees, independent contractors, clinical investigators, CROs, consultants and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates: (i) FDA regulations, including those laws requiring the reporting of true, complete and accurate information to the FDA, (ii) manufacturing standards, (iii) federal, state and foreign healthcare fraud and abuse laws, (iv) privacy protection laws or (v) laws that require the reporting of financial information or data accurately. Specifically, research, sales, marketing, education and other business arrangements in the healthcare industry are subject to extensive laws intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws may restrict or prohibit a wide range of pricing, discounting, education, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of business conduct and ethics, as well as various compliance policies and procedures, but it is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws. If any such actions are instituted against us, even if we are successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business. Violations of such laws subject us to numerous penalties, including, but not limited to, the imposition of civil, criminal and administrative penalties, damages, monetary fines, disgorgement, 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 San Diego, which in the past has experienced severe earthquakes. We do not carry earthquake insurance. The San Diego area has also experienced serious wildfires. If a natural disaster or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as product development and research efforts for our current product candidates and finance records, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and may not be adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

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

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

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. A severe or prolonged economic downturn may cause extreme volatility and disruptions in the capital and credit markets and could result in a variety of risks to our business and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers and third-party payors to delay making payments for our services.

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

Any of the foregoing could harm our business, and we cannot anticipate all the ways in which the current economic climate and financial market conditions could adversely impact our business.

Our business is subject to economic, political, regulatory, operational and other risks associated with international operations.

Our business is subject to risks associated with conducting business internationally. Some of our suppliers and collaborative relationships are located outside the United States, and we conduct some of our clinical trials outside the United States. Accordingly, our ability to operate our business and our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, or political instability in non-U.S. economies and markets;
- differing and changing regulatory or legal requirements in non-U.S. countries;
- challenges enforcing our contractual and intellectual property rights, especially in non-U.S. countries that may not respect and protect intellectual property rights to the same extent as the United States;
- difficulties in compliance with non-U.S. laws and regulations;
- changes in non-U.S. regulations and customs, tariffs and trade barriers;
- changes in currency exchange rates and non-U.S. currency controls;
- changes in a country's or region's political or economic environment;
- trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or non-U.S. governments;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty and labor unrest;
- difficulties associated with staffing and managing international operations;
- potential liability under the FCPA, UK Bribery Act or comparable non-U.S. laws; and

- business interruptions resulting from (i) geopolitical actions, including annexation, war and terrorism, (ii) natural disasters, including earthquakes, typhoons, floods and fires or (iii) outbreaks of health epidemics and pandemics.

Risks Related to Our Intellectual Property

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

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

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

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

Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after its effective filing date. Various extensions may be available; however, the life of a

patent, and the protection it affords, is limited. Without patent protection for our product or product candidates, we may be open to competition from generic versions of our product or product candidates. Further, if we encounter delays in our development efforts, including our clinical trials, the period of time during which we could market our product or product candidates under patent protection would be reduced.

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

In addition to the protection afforded by patents, we also rely on trade secret protection to protect proprietary know-how that may not be patentable or that we elect not to patent, processes for which patents may be difficult to obtain or enforce, and any other elements of our product and product candidates, and our product development processes (such as manufacturing and formulation technologies) that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect. If the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating any trade secrets. Misappropriation or unauthorized disclosure of our trade secrets could significantly affect our competitive position and may have a material adverse effect on our business. Furthermore, trade secret protection does not prevent competitors from independently developing substantially equivalent information and techniques, and we cannot guarantee that our competitors will not independently develop substantially equivalent information and techniques. The FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all.

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

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

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

For our U.S. patent and patent applications containing a claim not entitled to priority before March 16, 2013, there is a greater level of uncertainty in the patent law. In September 2011, the Leahy-Smith America Invents Act, or the America Invents Act (AIA), was signed into law. The AIA includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. It is not clear what other, if any, impact the AIA will have on the operation of our business. Moreover, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a “first-to-file” system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the USPTO after March 16, 2013 but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Furthermore, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our technology and the prior art allow our technology to be patentable over the prior art. Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to either (i) file any patent application related to our product or product candidates or (ii) invent any of the inventions claimed in our patents or patent applications.

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

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

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

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

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

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

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to pharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally in those countries. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. In addition, certain countries in Europe and certain other countries, including India and China, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we may have limited remedies if our patents are infringed or if we are compelled to grant a license to our patents to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license. Finally, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws.

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

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

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

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

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

Third parties may infringe or misappropriate our intellectual property, including our existing patents, patents that may issue to us in the future, or the patents of our licensors to which we have a license. As a result, we may be required to file infringement claims to stop third-party infringement or unauthorized use. Further, we may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

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

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

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

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

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential

information could be compromised by disclosure. In addition, during the course of litigation or administrative proceedings, there could be public announcements of the results of hearings, motions or other interim proceedings or developments or public access to related documents. If investors perceive these results to be negative, the market price for our common stock could be significantly harmed.

Although not involving issued U.S. patents covering our product or any of our product candidates, on April 17, 2015, we filed a request for interference between one of our U.S. pending applications and a U.S. pending application controlled by Auris Medical Holding AG (Auris). On July 20, 2015, we received notice from the USPTO that the Patent Trial and Appeal Board (PTAB) declared an interference between our pending application and the Auris patent (issued as U.S. Patent No. 9,066,865 on June 30, 2015). On January 26, 2017, the PTAB determined that all of the Otonomy patent claims and all but one of the Auris patent claims were not patentable. We filed a Notice of Appeal on March 27, 2017, in which we asked the Federal Circuit to reverse PTAB's decision that our claims are not patentable and that Auris's single claim is. On August 1, 2018, the Federal Circuit agreed with us that the PTAB had erred in its rulings for Auris. The court reversed the PTAB's decision against Otonomy and remanded the case for the PTAB to enter judgment for Otonomy. On March 11, 2019, the PTAB entered the judgment for Otonomy and cancelled the Auris patent. On April 24, 2020, the USPTO issued a Notice of Allowance for our pending application, indicating that all of our claims are allowed.

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

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

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

with any development or potential commercialization of OTO-313 and could subject us to claims of patent infringement by Durect if OTO-313 is covered by the licensed patents.

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

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

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

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

Risks Related to Government Regulation

Our business and products are subject to extensive government regulation.

We are subject to extensive, complex, costly and evolving regulation by federal and state governmental authorities in the United States, principally by the FDA, the U.S. Drug Enforcement Administration (DEA), the Centers for Disease Control and Prevention (CDC), the U.S. Department of Health and Human Services, and its various agencies, and also from state and foreign regulatory authorities. Failure to comply with all applicable regulatory requirements, including those promulgated under the Federal Food, Drug, and Cosmetic Act (FFDCA), the Public Health Service Act, and the Controlled Substances Act, among others, may subject us to operating restrictions and criminal prosecution, monetary penalties and other disciplinary actions, including, sanctions, warning letters, product seizures, recalls, fines, injunctions, suspension, revocation of approvals, disgorgement, contractual damages, and/or exclusion from future participation in the Medicare and Medicaid

programs. After our products receive regulatory approval or clearance, we, and our direct and indirect suppliers, remain subject to the periodic inspection of our plants and facilities, review of production processes, and testing of our products to confirm that we are in compliance with all applicable regulations. Adverse findings during regulatory inspections may result in the implementation of Risk Evaluation and Mitigation Strategies (REMS), programs, completion of government mandated clinical trials, and government enforcement action relating to labeling, advertising, marketing and promotion, as well as regulations governing cGMPs.

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

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

- warning letters and adverse publicity;
- civil and criminal penalties;
- injunctions;
- withdrawal of approved products;
- product seizure or detention;
- product recalls;
- total or partial suspension of production; and
- refusal to approve pending NDAs or supplements to approved NDAs.

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

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

Regulatory approval is not guaranteed, and the approval process is expensive and may take several years. The FDA also has substantial discretion in the approval process. Despite the time and

expense expended, failure can occur at any stage, and we could encounter problems that cause us to abandon or repeat clinical trials, or perform additional nonclinical studies and clinical trials. The number of nonclinical studies and clinical trials that will be required for FDA approval varies depending on the product candidate, the disease or condition that the product candidate is designed to address and the regulations applicable to any particular product candidate. The FDA can delay, limit or deny approval of a product candidate for many reasons, including the following:

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

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

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

If and when regulatory approval has been granted, our product candidates or any approved product will be subject to continual regulatory review by the FDA and/or non-U.S. regulatory authorities. Additionally, our product and any product candidates, if approved, will be subject to extensive and ongoing regulatory requirements, including labeling and other restrictions and market withdrawal, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products. Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indications for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product. In addition, for our product, and if the applicable regulatory agency approves our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include prompt submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP and GCP for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with our product or our product candidates, including adverse events of unanticipated severity or frequency, or problems with our third-party manufacturers' processes, or failure to comply with regulatory requirements, may result in, among other things:

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

Our ongoing regulatory requirements may also change from time to time, potentially harming or making costlier our commercialization efforts. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the

United States or other countries. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business.

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

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

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

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

Additionally, state and federal authorities have aggressively targeted medical technology and pharmaceutical companies for, among other things, alleged violations of these healthcare fraud and abuse statutes, based on, for example, improper research or consulting contracts and other services agreements with doctors, certain marketing arrangements that rely on volume-based pricing, off-label marketing schemes, and other improper promotional practices.

The federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH Act), and their implementing regulations, 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, U.S. and international laws and regulations could impact our ability to store and process personal data, use certain vendors or service providers, and utilize personal data from certain jurisdictions. Because the global privacy and data protection landscape is rapidly evolving, we may be affected by or subject to new, amended or existing laws and regulations in the future, including as our operations continue to expand or if we operate in foreign jurisdictions.

For example, in the United States, HIPAA imposes certain obligations, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without proper written authorization. Similarly, the California Consumer Privacy Act of 2018 (CCPA) took effect on January 1, 2020. The CCPA gives California residents the right to access and require deletion of their personal information, the right to opt out of certain personal information sharing, and the right to detailed information about how their personal information is collected, used and shared. The CCPA provides civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Although the CCPA includes exemptions for certain clinical trials data, the law may increase our compliance costs and potential liability with respect to other personal information we collect about California residents. The CCPA has prompted a wave of proposals for new federal and state privacy legislation that, if passed, could increase our potential liability, increase our compliance costs and adversely affect our business.

Several foreign jurisdictions, including the European Union, its member states, the United Kingdom, Japan and Australia, among others, have adopted legislation and regulations that increase or change the requirements governing the collection, use, disclosure and transfer of the personal information of individuals in these jurisdictions. Additionally, certain countries have passed or are considering passing laws that require local data residency and/or restrict the international transfer of data. These laws have the potential to increase costs of compliance, risks of noncompliance and penalties for noncompliance.

For example, the collection and use of health data in the EU is governed by the General Data Protection Regulation (GDPR). The GDPR extends the geographical scope of EU data protection law to non-EU entities under certain conditions, tightens existing EU data protection principles and creates new obligations for companies and new rights for individuals. Guidance, interpretation and application under the GDPR are still developing and may change over time. Failure to comply with the GDPR and the applicable national data protection laws of the EU member states may result in substantial fines and other administrative penalties. The GDPR may increase our responsibility and liability in relation to personal data that we control and/or process and we may be required to put in place additional mechanisms ensuring compliance with the GDPR. This may be onerous and if our efforts to comply with GDPR or other applicable EU laws and regulations are not successful, it could adversely affect our business in the EU.

Since the approval of OTIPRIO, our operations have been subject to the federal transparency requirements under the federal Physician Payment Sunshine Act, created under the ACA, which requires certain manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to annually report to CMS information related to payments and other transfers of value provided to physicians, as defined by law, and teaching hospitals and certain ownership and investment interests held by physicians and their immediate family members. Additionally, in 2018 the "Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act" was enacted which, under the provision entitled "Fighting the Opioid Epidemic with Sunshine," in part, extends the reporting and transparency requirements for physicians under the Physician Payments Sunshine Act to physician assistants, nurse practitioners and other mid-level practitioners, with reporting requirements going into effect in 2022 for payments made in 2021.

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

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

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

From time to time, legislation is drafted and introduced in Congress in the United States or by governments in foreign jurisdictions that could significantly change the statutory provisions governing the regulatory clearance or approval, manufacture, and marketing of regulated products or the reimbursement thereof. Further, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. In addition, FDA or foreign regulatory agency regulations and guidance are often revised or reinterpreted by the FDA or the applicable foreign regulatory agency in ways that may significantly affect our business and our product and product candidates. Any new regulations or revisions or reinterpretations of existing regulations may impose additional costs or lengthen review times of our product candidates or any future product candidates. We cannot determine what effect changes in regulations, statutes, legal interpretation or policies, when and if promulgated, enacted or adopted may have on our business in the future. Such changes could, among other things, require:

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

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

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

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

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

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

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the Office of Foreign Assets Control of the U.S. Department of the Treasury, the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, the UK Bribery Act 2010, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. U.S. economic sanctions and export control laws and regulations prohibit the shipment of certain products and services to countries, governments, and persons targeted by U.S. sanctions. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other partners from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector.

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

Risks Related to Ownership of Our Securities

The price of our common stock has been, is, and may continue to be highly volatile, which may make it difficult for stockholders to sell our common stock when desired or at attractive prices.

Our stock is currently traded on the Nasdaq Global Select Market, but we can provide no assurance that we will be able to maintain an active trading market on the Nasdaq Global Select Market or any other exchange in the future. Moreover, the trading price of our common stock may fluctuate substantially. These price fluctuations may be rapid and severe and may leave investors little time to react. Broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance. Sharp drops in the market price of our common stock may also expose us to securities class-action litigation.

We and the underwriters will determine the offering price of our common stock and the pre-funded warrants 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. The market price of our common stock has been and is likely to continue to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including:

- regulatory or legal developments;
- results from or delays in clinical trials of our product candidates or product candidates of companies that are perceived to be similar to us;
- announcements of regulatory approval or disapproval of our product candidates;
- commercialization of our products, if approved;
- FDA or other regulatory actions affecting us or our industry;
- introductions and announcements of new products or product candidates by us, any commercialization partners or our competitors, and the timing of these introductions and announcements;
- our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- announcements by us or our competitors of significant acquisitions, licenses, strategic partnerships, joint ventures or capital commitments;
- market conditions in the pharmaceutical and biopharmaceutical sectors and issuance of securities analysts' reports or recommendations;
- actual or anticipated quarterly variations in our results of operations or those of our competitors;
- changes in financial estimates or guidance, including our ability to meet our revenue, operating profit or loss and cash balance estimates or guidance;
- sales of substantial amounts of our stock by insiders and large stockholders, or the expectation that such sales might occur;
- general economic, industry and market conditions;
- the impact of any natural disasters or public health crises, such as the COVID-19 pandemic;
- additions or departures of key personnel;
- intellectual property, product liability or other litigation against us;
- expiration or termination of our potential relationships with strategic partners;
- limited trading volume of our common stock; and
- the other factors described in this "Risk Factors" section.

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

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

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

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

In September 2018, the registration statement on Form S-3 (File No. 333-227269) to which this prospectus supplement forms a part was declared effective by the SEC, pursuant to which we may offer debt securities, preferred stock, common stock and certain other securities from time to time, in addition to shares of our common stock sold pursuant to this offering. On August 1, 2019, we filed a prospectus supplement in connection with an "at the market" offering under our Sales Agreement with Cowen and Company, LLC, under which we may sell shares of common stock for up to an aggregate of $40.0 million. If in the future we issue additional shares of common stock or securities convertible into common stock, our common stockholders would experience additional dilution and, as a result, the market price of our common stock may decline. We cannot predict the effect that future sales of our common stock would have on the market price of our common stock. Additionally, investors may be further diluted by the exercise of the pre-funded warrants being offered in this offering.

We have agreed that for a period of 60 days after the date of this prospectus supplement, and our directors, executive officers and certain affiliates of our directors have agreed that for a period of 60 days after the date of this prospectus supplement, subject to specified exceptions, we or they will not offer, sell, contract to sell, pledge or otherwise dispose of, directly or indirectly, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock. Sales of stock by any of our directors, executive officers or principal stockholders could have a material adverse effect on the trading price of our common stock.

As of March 31, 2020, certain holders of approximately 4,192,638 shares of our common stock, including shares issuable upon the exercise of outstanding options, are entitled to certain rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by our affiliates as defined in Rule 144 under the Securities Act.

Any sales of securities by these stockholders could have a material adverse effect on the market price of our common stock.

We do not anticipate paying dividends on our capital stock.

We do not intend to pay dividends on our capital stock in the foreseeable future. The declaration of dividends is subject to the discretion of our board of directors and will depend on various factors, including our operating results, financial condition, future prospects and any other factors deemed relevant by our board of directors. You should not rely on an investment in our company if you require dividend income from your investment in our company. The success of your investment will likely depend entirely upon any future appreciation of the market price of our capital stock, which is uncertain and unpredictable. There is no guarantee that our capital stock will appreciate in value or even maintain the price at which you purchased your shares.

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

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

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

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

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

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

As of March 31, 2020, our executive officers, directors and current beneficial owners of 5% or more of our common stock, in aggregate, beneficially owned approximately 32.8% of our outstanding common stock. Accordingly, these stockholders, acting together, may significantly influence all matters requiring stockholder approval, including the election and removal of directors and any merger or other significant corporate transactions. These stockholders may therefore delay or prevent a change of control, even if such a change of control would benefit our other stockholders. The significant concentration of stock ownership may adversely affect the market price of our common stock due to investors' perception that conflicts of interest may exist or arise.

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

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

control transaction. As a result, the market price of our common stock and the voting and other rights of our stockholders may be adversely affected. An issuance of shares of preferred stock may result in the loss of voting control to other stockholders.

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

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

In addition, we are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. These provisions may also prevent changes in our management or limit the price that certain investors are willing to pay for our stock.

Our amended and restated certificate of incorporation and our amended and restated bylaws provide that the Court of Chancery of the State of Delaware and the federal district courts of the United States will be the exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the sole and exclusive forum for the following:

- any derivative action or proceeding brought on our behalf;
- any action or proceeding asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee of ours to us or our stockholders;
- any action or proceeding asserting a claim arising pursuant to any provision of the Delaware General Corporation Law or our amended- and restated certificate of incorporation or amended and restated bylaws; and
- any action or proceeding asserting a claim governed by the internal-affairs doctrine.

This provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act or any other claim for which the U.S. federal courts have exclusive jurisdiction.

Our amended and restated bylaws further provide that the federal district courts of the United States will be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act.

These exclusive-forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage lawsuits against us and our directors, officers and other employees. Any person or entity purchasing or otherwise acquiring any interest in any of our securities shall be deemed to have notice of and consented to these provisions. There is uncertainty as to whether a court would enforce such provisions, and the enforceability of similar choice of forum provisions in other companies' charter documents has been challenged in legal proceedings.

It is possible that a court could find these types of provisions to be inapplicable or unenforceable, and if a court were to find either exclusive-forum provision in our amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could seriously harm our business.

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

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

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

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

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

As of December 31, 2019, we had U.S. federal and state net operating loss carryforwards (NOLs) of approximately $337.4 million and $131.7 million, respectively. Of the federal NOLs, approximately $96.8 million were generated after January 1, 2018, and therefore do not expire. Our U.S. federal and state NOLs will expire in various years beginning in 2030, if not utilized. Under the 2017 legislation commonly referred to as the Tax Cuts and Jobs Act (the Tax Act), as modified by the Coronavirus Aid, Relief, and Economic Security Act (CARES Act), the deductibility of our federal NOLs generated in tax years beginning after December 31, 2020 will be limited to 80% of taxable income in such years. As of December 31, 2019, we had federal and California research and development tax credit carryforwards of approximately $10.9 million and $5.0 million, respectively. The federal research and development tax credit carryforwards expire in various years beginning in 2030, if not utilized. The California research credit will carry forward indefinitely. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," the corporation's ability to use its pre-change federal NOLs and other pre-change tax attributes, such as research tax credits, to offset its future post-change income and taxes may be limited. In general, an "ownership change" occurs if there is a cumulative change in our ownership by "5% shareholders" that exceeds 50 percentage points over a rolling three-year period. Similar rules may apply under state tax laws. We believe we have experienced certain ownership changes in the past and have reduced our deferred tax

assets related to NOLs and research and development tax credit carryforwards accordingly. In the event that it is determined that we have in the past experienced additional ownership changes, or if we experience one or more ownership changes as a result of future transactions in our stock, then we may be further limited in our ability to use our NOLs and other tax assets to reduce taxes owed on the net taxable income that we earn in the event that we attain profitability. Any such limitations on the ability to use our NOLs and other tax assets could adversely impact our business, financial condition and operating results in the event that we attain profitability.

The enactment of tax reform policies could adversely affect our business and financial condition.

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could adversely affect our business operations and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. For example, the Tax Act enacted many significant changes to the U.S. tax laws. Future guidance from the Internal Revenue Service and other tax authorities with respect to the Tax Act may affect us, and certain aspects of the Tax Act could be repealed or modified in future legislation. For example, the CARES Act modified certain provisions of the Tax Act. In addition, it is uncertain if and to what extent various states will conform to the Tax Act or any newly enacted federal tax legislation. Changes in corporate tax rates, the realization of net deferred tax assets relating to our operations, and the deductibility of expenses under the Tax Act or future reform legislation could have a material impact on the value of our deferred tax assets, could result in significant one-time charges, and could increase our future U.S. tax expense.

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, we incur and will continue to incur significant legal, accounting and other expenses. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure, including the Sarbanes-Oxley Act of 2002 (the Sarbanes-Oxley Act) and regulations implemented by the SEC, and The Nasdaq Stock Market (Nasdaq) may increase legal and financial compliance costs and make some activities more time consuming. These laws, regulations and standards are subject to varying interpretations and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities. If, notwithstanding our efforts to comply with new laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

As a public company in the United States, we are required, pursuant to the Sarbanes-Oxley Act, to maintain effective disclosure controls and procedures and internal control over financial reporting. We are also required to provide an annual management report on the effectiveness of our disclosure controls and procedures over financial reporting. We need to disclose any material weaknesses identified by our management in our internal control over financial reporting, and at any time when we are not a non-accelerated filer, 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. 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.

Our current controls, and any new controls that we develop may become inadequate because of changes in conditions in our business or the degree of compliance with these policies or procedures may deteriorate and significant deficiencies or 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, may 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. Any failure to develop or maintain effective controls or any difficulties encountered in their implementation could harm our results of operations or cause us to fail to meet our reporting obligations and may result in a restatement of our financial statements for prior periods. Any failure to implement and maintain effective internal control over financial reporting also could adversely affect the results of periodic management evaluations regarding the effectiveness of our internal control over financial reporting that are required to be included in our periodic reports that will be filed with the SEC. Ineffective disclosure controls and procedures and internal control over financial reporting could also cause investors to lose confidence in our reported financial information and operating results, which could result in a negative market reaction and effect on the trading price of our common stock.

We are a "smaller reporting company," and the reduced disclosure requirements applicable to smaller reporting companies could make our common stock less attractive to investors.

We are a "smaller reporting company," as defined in Rule 12b-2 of the Exchange Act. For as long as we remain a "smaller reporting 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 "smaller reporting 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; and
- reduced disclosure obligations regarding executive compensation.

We cannot predict whether investors will find our common stock less attractive as a result of our reliance on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and the market price of our common stock may be reduced or more volatile.

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

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

Additional Risks Related to This Offering

Management will have broad discretion as to the use of the proceeds from this offering and may not use the proceeds effectively.

Although we currently intend to use the net proceeds from this offering in the manner described in the section entitled "Use of Proceeds" in this prospectus supplement, our management will have broad

discretion as to the application of the net proceeds from this offering. Our management may use the net proceeds for corporate purposes that may not improve our financial condition or market value.

You may experience immediate and substantial dilution.

Because the price per share at which shares of our common stock and pre-funded warrants are sold in this offering may be substantially higher than the net tangible book value per share of our common stock outstanding prior to this offering, you may suffer immediate and substantial dilution in the net tangible book value of the common stock or pre-funded warrants you purchase in this offering. The exercise of outstanding stock options will result in further dilution of your investment. See the section titled “Dilution” below for a more detailed illustration of the dilution you would incur if you participate in this offering.

You may experience future dilution as a result of future equity offerings.

To the extent that we raise additional funds through the sale of equity or convertible debt securities, the issuance of such securities will result in dilution to our stockholders. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in this offering.

There is no public market for the pre-funded warrants being offered in this offering.

There is no public trading market for the pre-funded warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to list the pre-funded warrants on The Nasdaq Global Select Market or any other national securities exchange or nationally recognized trading system. Without an active trading market, the liquidity of the pre-funded warrants will be limited.

Holders of the pre-funded warrants will have no rights as common stockholders until such holders exercise their pre-funded warrants and acquire our common stock.

Until holders of the pre-funded warrants exercise their pre-funded warrants and acquire shares of our common stock, such holders will have no rights with respect to the shares of our common stock underlying such pre-funded warrants.

FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, the documents we have filed with the SEC that are incorporated by reference and any free writing prospectus that we have authorized for use in connection with this offering contain "forward-looking statements" within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act, that involve risks and uncertainties, as well as assumptions, that, if they never materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. All statements contained in this prospectus supplement and accompanying prospectus, other than statements of historical fact, including statements regarding our future results of operations and financial position, our business strategy and plans, and our objectives for future operations, are forward-looking statements. The words "believe," "may," "will," "potentially," "estimate," "continue," "anticipate," "intend," "could," "would," "project," "plan," "expect" and the negative and plural forms of these words and similar expressions are intended to identify forward-looking statements, but are not the exclusive means of identifying such statements.

These forward-looking statements may include, but are not limited to, statements concerning the following:

- our expectations regarding our clinical development of OTIVIDEX, including expectations for the enrollment and availability of top-line results from the ongoing Phase 3 clinical trial, acceptance and adequacy of the statistical analysis plan for such trial, and expectations that one additional successful pivotal trial is sufficient to support the United States registration of OTIVIDEX in Ménière's disease;
- the size of the market opportunity and the number of patients who suffer from the diseases and disorders we are targeting;
- our expectations regarding the clinical development of OTO-313, including future development activities;
- our expectations regarding the clinical development of OTO-413, including availability of top-line results from the ongoing Phase 1/2 clinical trial in hearing loss patients;
- our expectations regarding the potential impacts on our business, preclinical programs and clinical trials due to the COVID-19 pandemic;
- the timing or likelihood of regulatory filings and approvals;
- our expectations regarding the future development of other product candidates, including but not limited to our development plans for our OTO-510 and OTO-6XX programs;
- our expectations regarding our strategic collaboration with AGTC to develop and commercialize a gene therapy for congenital hearing loss;
- our expectations regarding OTIPRIO co-promotion partnerships;
- our plans regarding the use of contract manufacturers for the production of our product candidates for clinical trials and, if approved, commercial use;
- our plans and ability to effectively establish and manage our own sales and marketing capabilities, or seek and establish collaborative partners, to commercialize our products;
- our ability to advance product candidates into, and successfully complete, clinical trials;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- the initiation, timing, progress and results of future nonclinical studies and clinical trials;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- estimates of our expenses, future revenue, capital requirements and our needs for additional financing;

- estimates of our cash, cash equivalents and short-term investments following this offering;
- our financial performance;
- accounting principles, policies and estimates; and
- the intended use of any proceeds from this offering.

These forward-looking statements are subject to a number of risks, uncertainties, and assumptions, including but not limited to: delays and disruption resulting from the COVID-19 pandemic and governmental responses to the pandemic, including current and future impacts to our operations, our limited operating history and our expectation that we will incur significant losses for the foreseeable future; our ability to obtain additional financing; our dependence on the clinical, regulatory and commercial success of OTIVIDEX and advancement of additional product candidates, such as OTO-313 and OTO-413, through clinical development to regulatory approval and commercialization, the uncertainties inherent in the clinical drug development process, including, without limitation, our ability to adequately demonstrate the safety and efficacy of our product candidates, the nonclinical and clinical results for our product candidates, which may not support further development, and challenges related to patient enrollment in clinical trials; our ability to obtain regulatory approval for our product candidates; side effects or adverse events associated with our product candidates; competition in the biopharmaceutical industry; our dependence on third parties to conduct nonclinical studies and clinical trials; our dependence on third parties for the manufacture of OTIPRIO and our product candidates; our ability to protect our intellectual property related to OTIPRIO and our product candidates in the United States and throughout the world; expectations regarding potential market size, opportunity and growth; our ability to manage operating expenses; implementation of our business model and strategic plans for our business, product candidates and technology; the risk of the occurrence of any event, change or other circumstance that could give rise to the termination of promotional or collaboration agreements; the risks of the occurrence of any event, change or other circumstances that could impact our ability to repay or comply with the terms of the loan provided by Oxford Finance LLC; and other risks. These forward-looking statements reflect our beliefs and views with respect to future events and are based on estimates and assumptions as of the date of this prospectus supplement and are subject to risks and uncertainties.

We discuss many of these risks in greater detail in the section titled “Risk Factors” included in this prospectus supplement beginning on page S-9. Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make.

Given these uncertainties, you should not place undue reliance on these forward-looking statements. We qualify all the forward-looking statements in this prospectus supplement by these cautionary statements. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in any forward-looking statements, whether as a result of new information, future events or otherwise.

You should read this prospectus supplement, the accompanying prospectus, the documents we have filed with the SEC that are incorporated by reference and any free writing prospectus that we have authorized for use in connection with this offering completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements.

MARKET, INDUSTRY AND OTHER DATA

This prospectus supplement and the documents incorporated by reference in this prospectus supplement contain estimates, projections and other information concerning our industry, our business and the markets for our product candidates, including data regarding the estimated size of such markets and the incidence of certain medical conditions. We obtained the industry, market and similar data in this prospectus supplement and the documents incorporated by reference in this prospectus supplement from our internal estimates and research, including surveys and studies we have sponsored and/or conducted, and from academic and industry research, publications, surveys and studies conducted by third parties, including governmental agencies. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. While we believe that the data we use from third parties are reliable, we have not separately verified these data. Further, while we believe our internal research is reliable, such research has not been verified by any third party. You are cautioned not to give undue weight to any such information, projections and estimates.

USE OF PROCEEDS

We estimate that the net proceeds from this offering will be approximately $55.8 million based on the sale by us of 14,500,000 shares of our common stock and pre-funded warrants to purchase 4,000,000 shares of our common stock, or approximately $64.2 million if the underwriters exercise in full their option to purchase an additional 2,775,000 shares of common stock, at the public offering price of $3.25 per share of common stock and $3.249 per pre-funded warrant, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We currently intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and short-term investments, to fund the development of OTIVIDEX, including completion of our ongoing Phase 3 clinical trial and, based on the results, submission of an NDA with the FDA; the Phase 2 clinical development program for OTO-313; the development of OTO-413, including our ongoing Phase 1/2 clinical trial and, based on the results, the initiation of a Phase 2 clinical trial; further advancement of our other programs including our GJB2 gene therapy program; and the remainder for other research and development activities, working capital, and other general corporate purposes. We may also use a portion of the net proceeds from this offering and our existing cash, cash equivalents and short-term investments to in-license, acquire or invest in complementary business, technologies, products or assets. However, we have no current plans, commitments or obligations to do so.

This expected use of the net proceeds from the offering represents our intentions based upon our current plans and business conditions. We cannot specify with certainty all of the particular uses of the net proceeds that we will receive from this offering, or the amounts that we will actually spend on the uses set forth above. The amounts and timing of our actual expenditures will depend on numerous factors, including the ongoing status of and results from clinical trials and other studies, the product approval process with the FDA, and the scope of our commercialization efforts, as well as any strategic collaborations that we may enter into with third parties for our product candidates, any unforeseen cash needs, and our investments and acquisitions. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in using these proceeds. Investors will be relying on our judgment regarding the use of the net proceeds from this offering. We believe that our existing cash, cash equivalents and short-term investments together with the net proceeds of this proposed offering will be sufficient to fund our operations for at least twelve months from the date of this prospectus supplement.

Pending the use of proceeds as described above, we plan to invest the net proceeds that we receive in short-term and intermediate-term interest-bearing obligations, investment-grade investments, certificates of deposit or direct or guaranteed obligations of the U.S. government. We cannot predict whether the invested proceeds will yield a favorable return.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our common stock and do not currently anticipate declaring or paying cash dividends on our common stock in the foreseeable future. We currently intend to retain all of our future earnings, if any, to fund the development and growth of our business. In addition, our Loan and Security Agreement, dated December 31, 2018, among the Company, Oxford Finance LLC, as collateral agent, and the lenders party thereto from time to time, and future debt instruments we issue may restrict our ability to pay dividends on our common stock. Any future determination relating to our dividend policy will be made at the discretion of our board of directors and will depend on a number of factors, including future earnings, capital requirements, financial conditions, future prospects, contractual restrictions and other factors that our board of directors may deem relevant.

DILUTION

If you invest in our common stock or pre-funded warrants in this offering, your interest will be diluted to the extent of the difference between the price per share of our common stock or pre-funded warrant you pay in this offering and the as adjusted net tangible book value per share of our common stock immediately after this offering.

Our net tangible book value as of March 31, 2020 was approximately $29.9 million, or $0.97 per share of our common stock. Net tangible book value per share is determined by dividing our total tangible assets, less total liabilities, by the number of shares of our common stock outstanding as of March 31, 2020. Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the as adjusted net tangible book value per share of our common stock immediately after giving effect to this offering.

After giving effect to the sale of our common stock and pre-funded warrants in this offering at the public offering price of $3.25 per share of common stock and $3.249 per pre-funded warrant (which equals the price per share at which shares of common stock are being sold to the public in this offering, minus the $0.001 per share exercise price of each such pre-funded warrant), including shares of common stock issuable upon exercise of the pre-funded warrants but excluding any resulting accounting associated therewith, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of March 31, 2020 would have been approximately $85.7 million, or $1.74 per share. This represents an immediate increase in net tangible book value of $0.77 per share to existing stockholders and immediate dilution in net tangible book value of $1.51 per share to new investors purchasing our common stock and pre-funded warrants in this offering.

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

Public offering price per share of common stock		$3.25
Net tangible book value per share as of March 31, 2020	$0.97	
Increase in net tangible book value per share attributable to new investors	0.77	
As adjusted net tangible book value per share after this offering		1.74
Dilution per share to investors in this offering		$1.51

The foregoing table and calculations are based on 30,814,211 shares of our common stock outstanding as of March 31, 2020, assumes the full exercise of the pre-funded warrants and excludes:

- 10,052,847 shares of our common stock issuable upon the exercise of options outstanding as of March 31, 2020, with a weighted-average exercise price of $4.19 per share;
- 2,531,206 shares of our common stock reserved for future issuance as of March 31, 2020 under our 2014 Equity Incentive Plan;
- 2,439,428 shares of our common stock reserved for issuance as of March 31, 2020 under our employee stock purchase plan; and
- shares of our common stock that may be sold from time to time under an “at the market” equity offering program that we entered into on August 1, 2019 with Cowen and Company, LLC, of which no shares have been sold to date.

Unless otherwise indicated, all information in this prospectus supplement assumes no exercise of outstanding options after March 31, 2020.

If the underwriters exercise in full their option to purchase up to 2,775,000 additional shares of common stock at the public offering price of $3.25 per share, the as adjusted net tangible book value after this offering (including shares issuable upon the exercise of the pre-funded warrant but excluding any resulting accounting associated therewith and after deducting underwriting discounts and commissions and estimated expenses payable by us) would be $1.81 per share, representing an increase in net tangible book value of $0.84 per share to existing stockholders and immediate dilution in net tangible book value of $1.44 per share to investors purchasing our common stock and pre-funded warrants in this offering at the public offering price.

To the extent that outstanding options are exercised, investors purchasing our common stock or pre-funded warrants in this offering will experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

DESCRIPTION OF PRE-FUNDED WARRANTS

The following is a brief summary of certain terms and conditions of the pre-funded warrants being offered in this offering. The following description is subject in all respects to the provisions contained in the pre-funded warrants.

Form

The pre-funded warrants will be issued as individual warrant agreements to the purchasers. The form of pre-funded warrant will be filed as an exhibit to a Current Report on Form 8-K that we expect to file with the SEC.

Term

The pre-funded warrants will expire on the date the warrant is exercised in full.

Exercisability

The pre-funded warrants are exercisable at any time after their original issuance. The pre-funded warrants will be exercisable, at the option of each holder, in whole or in part by delivering to us a duly executed exercise notice and by payment in full of the exercise price in immediately available funds for the number of shares of Common Stock purchased upon such exercise. As an alternative to payment in immediately available funds, the holder may, in its sole discretion, elect to exercise the pre-funded warrant through a cashless exercise, in which the holder would receive upon such exercise the net number of shares of our common stock determined according to the formula set forth in the pre-funded warrant. No fractional shares of our common stock will be issued in connection with the exercise of a pre-funded warrant. In lieu of fractional shares, we will pay the holder an amount in cash equal to the fractional amount multiplied by the last closing trading price of our common stock on the exercise date.

Exercise Limitations

We may not effect the exercise of any pre-funded warrant, and a holder will not be entitled to exercise any portion of any pre-funded warrant that, upon giving effect to such exercise, would cause: (i) the aggregate number of shares of our common stock beneficially owned by such holder (together with its affiliates) to exceed 9.99% of the number of shares of our common stock outstanding immediately after giving effect to the exercise; or (ii) the combined voting power of our securities beneficially owned by such holder (together with its affiliates) to exceed 9.99% of the combined voting power of all of our securities outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants. However, any holder of a pre-funded warrant may increase or decrease such percentage to any other percentage not in excess of 19.99% upon at least 61 days' prior notice from the holder to us.

Exercise Price

The exercise price of our common stock purchasable upon the exercise of the pre-funded warrants is $0.001 per share. The exercise price of the pre-funded warrants and the number of shares of our common stock issuable upon exercise of the pre-funded warrants is subject to appropriate adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common stock, as well as upon any distribution of assets, including cash, stock or other property, to our stockholders.

Transferability

Subject to applicable laws, the pre-funded warrants may be offered for sale, sold, transferred or assigned without our consent.

Exchange Listing

There is no established trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to apply for the listing of the pre-funded warrants on The Nasdaq Global Select Market, any other national securities exchange or any other nationally recognized trading system.

Fundamental Transactions

Upon the consummation of a fundamental transaction (as described in the pre-funded warrants, and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common stock, or any person or group becoming the beneficial owner of 50% of the voting power of our outstanding common stock), the holders of the pre-funded warrants will be entitled to receive, upon exercise of the pre-funded warrants, the kind and amount of securities, cash or other property that such holders would have received had they exercised the pre-funded warrants immediately prior to such fundamental transaction, without regard to any limitations on exercise contained in the pre-funded warrants.

No Rights as a Stockholder

Except by virtue of such holder’s ownership of shares of our common stock, the holder of a pre-funded warrant does not have the rights or privileges of a holder of our common stock, including any voting rights, until such holder exercises the pre-funded warrant.

MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES

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

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

- banks, insurance companies or other financial institutions;
- persons subject to the alternative minimum tax or the tax on net investment income;
- tax-exempt organizations;
- controlled foreign corporations, passive foreign investment companies and corporations that accumulate earnings to avoid U.S. federal income tax;
- dealers in securities or currencies;
- traders in securities that elect to use a mark-to-market method of accounting for their securities holdings;
- persons that own, or are deemed to own, more than five percent of our common stock and/or pre-funded warrants (except to the extent specifically set forth below);
- certain former citizens or long-term residents of the United States;
- persons who hold our common stock or pre-funded warrants as a position in a hedging transaction, "straddle," "conversion transaction" or other risk reduction transaction;
- persons who hold or receive our common stock pursuant to the exercise of any option or otherwise as compensation;
- persons who do not hold our common stock or pre-funded warrants as a capital asset within the meaning of Section 1221 of the Code;
- persons deemed to sell our common stock or pre-funded warrants under the constructive sale provisions of the Code; or
- persons required under Section 451(b) of the Code to conform the timing of any income accruals with respect to our common stock or pre-funded warrants on their financial statements.

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

You are urged to consult your tax advisor with respect to the application of the U.S. federal income tax laws to your particular situation, as well as any tax consequences of the purchase,

ownership and disposition of our common stock or pre-funded warrants, arising under the U.S. federal estate or gift tax laws or under the laws of any state, local, non-U.S. or other taxing jurisdiction or under any applicable tax treaty.

U.S. Holder and Non-U.S. Holder Defined

For purposes of this discussion, you are a U.S. holder if you are a beneficial owner of our common stock or pre-funded warrants that is any of the following (or treated as any of the following) and is not a partnership (or other entity classified as a partnership for U.S. federal income tax purposes):

- an individual citizen or resident of the United States (for U.S. federal income tax purposes);
- a corporation or other entity taxable as a corporation created or organized in the United States or under the laws of the United States or any political subdivision thereof;
- an estate whose income is subject to U.S. federal income tax regardless of its source; or
- a trust (x) whose administration is subject to the primary supervision of a U.S. court and that has one or more U.S. persons who have the authority to control all substantial decisions of the trust or (y) that has made a valid election under applicable Treasury Regulations to be treated as a U.S. person.

For purposes of this discussion, you are a non-U.S. holder if you are a beneficial owner of our common stock or pre-funded warrants that is not a U.S. holder, a partnership (or other entity classified as a partnership for U.S. federal income tax purposes), or a partner in a partnership.

General Treatment of Pre-Funded Warrants

Although the law in this area is not completely settled, the pre-funded warrants are generally expected to be treated as shares of our common stock for U.S. federal income tax purposes and a holder of pre-funded warrants should generally be taxed in the same manner as a holder of common stock as described below. You should discuss with your tax advisor the consequences of the acquisition, ownership and disposition of the pre-funded warrants, as well as the exercise of, certain adjustments to, and any payments in respect of the pre-funded warrants (including potential alternative characterizations). The balance of this discussion generally assumes that the characterization described above is respected for U.S. federal income tax purposes.

Tax Considerations Applicable to U.S. Holders

Distributions

As described above under “Dividend Policy,” we do not currently anticipate declaring or paying cash dividends on our common stock in the foreseeable future. However, if we do make distributions on our common stock, those payments will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed both our current and our accumulated earnings and profits, the excess will constitute a return of capital and will first reduce your basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock as described below under “Tax Considerations Applicable to U.S. Holders—Gain on Disposition of Common Stock or Pre-Funded Warrants.” If certain requirements are met, a preferential U.S. federal income tax rate will apply to any dividends paid to a beneficial owner of our common stock who is a non-corporate U.S. holder and meets certain holding period requirements.

Distributions constituting dividends for U.S. federal income tax purposes that are made to U.S. holders that are corporate shareholders may qualify for the dividends received deduction, or DRD, which is generally available to corporate shareholders. No assurance can be given that we will have sufficient earnings and profits (as determined under U.S. federal income tax principles) to cause any distributions to be eligible for a DRD. In addition, a DRD is available only if certain holding periods and other taxable income requirements are satisfied.

The taxation of a distribution received with respect to a pre-funded warrant is unclear. It is possible such a distribution would be treated as a distribution as described in this section, although other treatments may also be possible. U.S. holders should consult their tax advisors regarding the proper treatment of any payments in respect of the pre-funded warrants.

Gain on Disposition of Our Common Stock or Pre-Funded Warrants

Upon a sale or other taxable disposition of our common stock or pre-funded warrants, a U.S. holder generally will recognize capital gain or loss in an amount equal to the difference between the amount realized and the U.S. holder's adjusted tax basis in the common stock or pre-funded warrant. Capital gain or loss will constitute long-term capital gain or loss if the U.S. holder's holding period for the common stock or pre-funded warrant exceeds one year. The deductibility of capital losses is subject to certain limitations. U.S. holders who recognize losses with respect to a disposition of our common stock or pre-funded warrants should consult their own tax advisors regarding the tax treatment of such losses.

Exercise of Pre-Funded Warrants

As discussed above under the section titled "Description of Pre-Funded Warrants—Exercisability," a U.S. holder may exercise the pre-funded warrant by payment of exercise price or through a cashless exercise. The U.S. federal income tax treatment of a cashless exercise of pre-funded warrants into our common stock is unclear, and U.S. holders should consult their own tax advisors regarding the U.S. federal income tax consequences of a cashless exercise of pre-funded warrants. In general, however, a U.S. holder should not recognize gain or loss for U.S. federal income tax purposes upon exercise of a pre-funded warrant pursuant to either method, except to the extent the U.S. holder receives a cash payment for a fractional share that would otherwise have been issuable upon exercise of the pre-funded warrant, which will be treated as a sale subject to the rules described above under "Tax Considerations Applicable to U.S. Holders—Gain on Disposition of Our Common Stock or Pre-Funded Warrants." The U.S. holder's initial tax basis in the share of common stock received upon exercise of the pre-funded warrant generally should be equal to the sum of (i) such U.S. Holder's tax basis in the pre-funded warrant and (ii) the exercise price paid or treated as paid by the U.S. holder on the exercise of the pre-funded warrant. The U.S. holder's holding period in the common stock received upon exercise generally should include the U.S. Holder's holding period in the pre-funded warrants exchanged therefor.

Certain Adjustments to the Pre-Funded Warrants

Under Section 305 of the Code, an adjustment to the number of shares of common stock that will be issued on the exercise of the pre-funded warrants, or an adjustment to the exercise price of the pre-funded warrants, may be treated as a constructive distribution to a U.S. holder of the pre-funded warrants if, and to the extent that, such adjustment has the effect of increasing such U.S. holder's proportionate interest in our earnings and profits or assets, depending on the circumstances of such adjustment (for example, if such adjustment is to compensate for a distribution of cash or other property to our shareholders).

Information Reporting and Backup Withholding

Information reporting requirements generally will apply to payments of dividends (including constructive dividends) on the common stock and to the proceeds of a sale or other disposition of common stock or pre-funded warrants paid by us to a U.S. holder unless such U.S. holder is an exempt recipient, such as a corporation. Backup withholding at a current rate of 24% will apply to those payments if the U.S. holder fails to provide the U.S. holder's taxpayer identification number, or certification of exempt status, or if the U.S. holder otherwise fails to comply with applicable requirements to establish an exemption.

Backup withholding is not an additional tax. Rather, any amounts withheld under the backup withholding rules will be allowed as a refund or a credit against the U.S. holder's U.S. federal income tax liability provided the required information is timely furnished to the IRS. U.S. holders should consult their own tax advisors regarding their qualification for exemption from information reporting and backup withholding and the procedure for obtaining such exemption.

Tax Considerations Applicable to Non-U.S. Holders

Distributions

As described above under "Dividend Policy," we do not currently anticipate declaring or paying cash dividends on our common stock in the foreseeable future. However, if we do make distributions on our common stock, those payments will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed both our current and our accumulated earnings and profits, the excess will constitute a return of capital and will first reduce your basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock as described below under "—Gain on Disposition of Common Stock or Pre-Funded Warrants."

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

Dividends received by you that are effectively connected with your conduct of a U.S. trade or business (and, if required by an applicable income tax treaty, are attributable to a permanent establishment maintained by you in the United States) are includible in your gross income in the taxable year received, and are generally exempt from such withholding tax, subject to the discussions below on backup withholding and foreign accounts. In order to obtain this exemption, you must provide us or the applicable paying agent with an IRS Form W-8ECI or other applicable IRS Form W-8 properly certifying qualification for such exemption. Such effectively connected dividends, although not subject to withholding tax, are taxed at the same rates applicable to U.S. persons, net of certain deductions and credits, subject to an applicable income tax treaty providing otherwise. In addition, if you are a corporate non-U.S. holder, dividends you receive that are effectively connected with your conduct of a U.S. trade or business may also be subject to a branch profits tax at a rate of 30% or such lower rate as may be specified by an applicable income tax treaty. You should consult your tax advisor regarding any applicable tax treaties that may provide for different rules.

The taxation of a distribution received with respect to a pre-funded warrant is unclear. It is possible such a distribution would be treated as a distribution as described in this section, although other treatments may also be possible. Non-U.S. holders should consult their tax advisors regarding the proper treatment of any payments in respect of the pre-funded warrants.

Gain on Disposition of Common Stock or Pre-Funded Warrants

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

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

We believe that we are not currently, and do not currently expect to become a USRPHC. However, because the determination of whether we are a USRPHC depends on the fair market value of our U.S. real property relative to the fair market value of our other business assets, there can be no assurance that we will not become a USRPHC in the future. Even if we were to become a USRPHC, however, as long as our common stock is regularly traded on an established securities market, your common stock would be treated as a U.S. real property interest only if you actually or constructively held more than five percent of such regularly traded common stock at any time during the shorter of the five-year period preceding your disposition of, or your holding period for, our common stock. Special rules may apply to non-U.S. holders of pre-funded warrants, who should consult their tax advisors.

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

Exercise of Pre-Funded Warrants

As discussed above under the section titled "Description of Pre-Funded Warrants—Exercisability," a non-U.S. holder may exercise the pre-funded warrant by payment of the exercise price or through a cashless exercise. The U.S. federal income tax treatment of a cashless exercise of pre-funded warrants into our common stock is unclear, and non-U.S. holders should consult their own tax advisors regarding the U.S. federal income tax consequences of a cashless exercise of pre-funded warrants. In general, however, a non-U.S. holder should not recognize gain or loss for U.S. federal income tax purposes upon exercise of a pre-funded warrant pursuant to either method, except to the extent the non-U.S. holder receives a cash payment for a fractional share that would otherwise have been issuable upon exercise of the pre-funded warrant, which will be treated as a sale subject to the rules described above under "Tax Considerations Applicable to Non-U.S. Holders—Gain on Disposition of Our Common Stock or Pre-Funded Warrants."

Certain Adjustments to the Pre-Funded Warrants

Under Section 305 of the Code, an adjustment to the number of shares of common stock that will be issued on the exercise of the pre-funded warrants, or an adjustment to the exercise price of the pre-

funded warrants, may be treated as a constructive distribution to a Non-U.S. holder of the pre-funded warrants if, and to the extent that, such adjustment has the effect of increasing such Non-U.S. holder's proportionate interest in our "earnings and profits" or assets, depending on the circumstances of such adjustment (for example, if such adjustment is to compensate for a distribution of cash or other property to our shareholders).

Backup Withholding and Information Reporting

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

Payments of dividends or of proceeds on the disposition of common stock or pre-funded warrants made to you may be subject to information reporting and backup withholding at a current rate of 24% unless you establish an exemption, for example, by properly certifying your non-U.S. status on an IRS Form W-8BEN or W-8BEN-E (or another appropriate version of IRS Form W-8) or you otherwise meet the documentary evidence requirements for establishing that you are not a U.S. person or otherwise establish an exemption. Notwithstanding the foregoing, backup withholding and information reporting may apply if either we or the applicable paying agent has actual knowledge, or reason to know, that you are a U.S. person.

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

Foreign Accounts

Code Sections 1471-1474, commonly referred to as the Foreign Account Tax Compliance Act, or FATCA, and the Treasury Regulations issued thereunder generally impose a U.S. federal withholding tax of 30% on dividends on, and, subject to the proposed Treasury Regulations discussed below, the gross proceeds from a sale or other disposition of, our common stock or pre-funded warrants, paid to a "foreign financial institution" (as specially defined under these rules), unless such institution enters into an agreement with the U.S. government to, among other things, withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding the U.S. account holders of such institution (which include certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with U.S. owners) or otherwise establishes an exemption. FATCA also generally imposes a U.S. federal withholding tax of 30% on dividends on, and, subject to the proposed Treasury Regulations discussed below, the gross proceeds from a sale or other disposition of, our common stock or pre-funded warrants paid to a "non-financial foreign entity" (as defined under these rules) unless such entity provides the withholding agent with a certification identifying the direct and indirect U.S. owners of the entity, certifies that it does not have any substantial U.S. owners, or otherwise establishes an exemption. The withholding obligations under FATCA generally apply to dividends on our common stock or pre-funded warrants. The U.S. Department of the Treasury has issued proposed Treasury Regulations providing that, if finalized in their present form, the withholding obligations under FATCA would not apply with respect to payment of gross proceeds from a sale or other disposition of common stock or pre-funded warrants. The proposed Treasury Regulations may be relied upon until final Treasury Regulations are issued. Under certain circumstances, a non-U.S. holder might be eligible for refunds or credits of taxes withheld under FATCA. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this paragraph. Prospective investors are encouraged to consult with their own tax advisors regarding the possible implications of FATCA on their investment in our common stock or pre-funded warrants.

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

UNDERWRITING

We and the underwriters for the offering named below have entered into an underwriting agreement with respect to the common stock and pre-funded warrants being offered. Subject to the terms and conditions of the underwriting agreement, each underwriter has severally agreed to purchase from us the number of shares of our common stock and pre-funded warrants set forth opposite its name below. Cowen and Company, LLC and Piper Sandler & Co. are the representatives of the underwriters.

Underwriter	Number of Shares	Number of Pre-Funded Warrants
Cowen and Company, LLC	6,235,000	1,720,000
Piper Sandler & Co.	5,510,000	1,520,000
Cantor Fitzgerald & Co.	2,030,000	560,000
H.C. Wainwright & Co., LLC	725,000	200,000
Total	14,500,000	4,000,000

The underwriting agreement provides that the obligations of the underwriters are subject to certain conditions precedent and that the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of these shares or pre-funded warrants are purchased, other than those shares and pre-funded warrants covered by the option to purchase additional shares described below. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against specified liabilities, including liabilities under the Securities Act of 1933, as amended, or Securities Act, and to contribute to payments the underwriters may be required to make in respect thereof.

The underwriters are offering the shares and pre-funded warrants, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel and other conditions specified in the underwriting agreement. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Option to Purchase Additional Shares. We have granted to the underwriters an option to purchase up to 2,775,000 additional shares of common stock at the public offering price, less the underwriting discounts and commissions. This option is exercisable for a period of 30 days. To the extent that the underwriters exercise this option, the underwriters will purchase additional shares from us in approximately the same proportion as shown in the table above.

Discounts and Commissions. The following table shows the public offering price, underwriting discounts and commissions and proceeds, before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

We estimate that the total expenses of the offering, excluding underwriting discount, will be approximately $600,000 and are payable by us. We have agreed to reimburse the underwriters for certain of their expenses in an amount up to $25,000.

	Per Share	Per Pre-Funded Warrant	Total Without Exercise of Option to Purchase Additional Shares	Total With Full Exercise of Option to Purchase Additional Shares
Public offering price	$ 3.250000	$ 3.249000	$ 60,121,000.00	$ 69,139,750.00
Underwriting discounts and commissions	$ 0.203125	$ 0.203125	$ 3,757,812.50	$ 4,321,484.38
Proceeds, before expenses, to us	$ 3.046875	$ 3.045875	$ 56,363,187.50	$ 64,818,265.63

We are offering to those purchasers whose purchase of shares of common stock in this offering would result in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 9.99% of our outstanding common stock following the consummation of this offering, the opportunity to purchase, in lieu of the shares of our common stock that would result in ownership in excess of 9.99%, pre-funded warrants to purchase such excess shares of our common stock. Each pre-funded warrant will have an exercise price of $0.001. The purchase price for each such pre-funded warrant equals the per share public offering price for the common stock in this offering less the $0.001 per share exercise price of each such pre-funded warrant.

The underwriters propose to offer the shares of common stock and pre-funded warrants to the public at the public offering price set forth on the cover of this prospectus supplement. The underwriters may offer the shares of common stock and pre-funded warrants to securities dealers at the public offering price less a concession not in excess of $0.121875 per share of common stock and $0.121875 per pre-funded warrant. If all of the shares are not sold at the public offering price, the underwriters may change the offering price and other selling terms.

Discretionary Accounts. The underwriters do not intend to confirm sales of the shares or pre-funded warrants to any accounts over which they have discretionary authority.

Our common stock is listed on the Nasdaq Global Select Market under the symbol “OTIC.” There is no established public trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on the Nasdaq Global Select Market, any other national securities exchange or any other nationally recognized trading system.

Stabilization. In connection with this offering, the underwriters may engage in stabilizing transactions, overallotment transactions, syndicate covering transactions, penalty bids and purchases to cover positions created by short sales.

- Stabilizing transactions permit bids to purchase shares of common stock so long as the stabilizing bids do not exceed a specified maximum, and are engaged in for the purpose of preventing or retarding a decline in the market price of the common stock while the offering is in progress.
- Overallotment transactions involve sales by the underwriters of shares of common stock in excess of the number of shares the underwriters are obligated to purchase. This creates a syndicate short position which may be either a covered short position or a naked short position. In a covered short position, the number of shares over-allotted by the underwriters is not greater than the number of shares that they may purchase in the option to purchase additional shares. In a naked short position, the number of shares involved is greater than the

number of shares in the option to purchase additional shares. The underwriters may close out any short position by exercising their option to purchase additional shares and/or purchasing shares in the open market.

- Syndicate covering transactions involve purchases of common stock in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared with the price at which they may purchase shares through exercise of the option to purchase additional shares. If the underwriters sell more shares than could be covered by exercise of the option to purchase additional shares and, therefore, have a naked short position, the position can be closed out only by buying shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that after pricing there could be downward pressure on the price of the shares in the open market that could adversely affect investors who purchase in the offering.
- Penalty bids permit the representatives to reclaim a selling concession from a syndicate member when the common stock originally sold by that syndicate member is purchased in stabilizing or syndicate covering transactions to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock in the open market may be higher than it would otherwise be in the absence of these transactions. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of our common stock. These transactions may be effected on the Nasdaq Stock Market, in the over-the-counter market or otherwise and, if commenced, may be discontinued at any time.

Passive Market Making. In connection with this offering, underwriters and selling group members may engage in passive market making transactions in our common stock on the Nasdaq Stock Market in accordance with Rule 103 of Regulation M under the Securities Exchange Act of 1934, as amended, during a period before the commencement of offers or sales of common stock and extending through the completion of the distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, such bid must then be lowered when specified purchase limits are exceeded.

Lock-Up Agreements. Pursuant to certain "lock-up" agreements, we and our executive officers, directors and certain of our affiliated stockholders, have agreed, subject to certain exceptions, not to, and will not cause or direct any of its affiliates to, (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, hedge, lend or otherwise transfer or dispose of, directly or indirectly, or file with the SEC a registration statement under the Securities Act relating to, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock or (ii) enter into any swap, hedging or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of our shares of common stock or any such other securities, whether any such transaction described in clause (i) or (ii) above is to be settled by delivery of shares of our common stock or such other securities, in cash or otherwise, or publicly disclose the intention to undertake any of the foregoing, in each case without the prior written consent of Cowen and Company, LLC and Piper Sandler & Co., for a period of 60 days after the date of the pricing of the offering for our executive officers, directors and certain of our affiliated stockholders and a period of 60 days after the date of the pricing of the offering for us.

The exceptions permit us, among other things and subject to restrictions, to: (i) issue securities to be sold in this offering and the delivery of warrant shares upon exercise of the warrants, (ii) issue shares of our common stock upon the exercise of options granted under our existing equity incentive plans or warrants described as outstanding in the registration statement of which this prospectus supplement forms a part, provided that we shall use commercially reasonable efforts to cause the recipient of such shares of our common stock issued pursuant to this clause (ii) during the 60-day restricted period described above to enter into a lock-up agreement, (iii) grant options and other awards under an equity incentive plan described in the registration statement of which this prospectus supplement forms a part, (iv) file any registration statement on Form S-8 or a successor form thereto relating to an equity incentive plan described in the registration statement of which this prospectus supplement forms a part, and (v) issue shares of our common stock or other securities in connection with a transaction with an unaffiliated third party that includes a bona fide commercial relationship (including joint ventures, marketing or distribution arrangements, collaboration agreements or intellectual property license agreements) or any acquisition of assets or acquisition of not less than a majority or controlling portion of the equity of another entity, provided that (x) the aggregate number of shares issued pursuant to this clause (v) shall not exceed five percent (5%) of the total number of outstanding shares of common stock immediately following the issuance and sale of the shares of common stock and pre-funded warrants in this offering and (y) the recipient of any such shares of common stock and securities issued pursuant to this clause (v) during the 60-day restricted period described above shall enter into a lock-up agreement.

The exceptions permit parties to the “lock-up” agreements, among other things and subject to restrictions, to: (i) acquire shares of our common stock in open market transactions on or after the date of this prospectus supplement, provided that no filing by any party (donor, donee, transferor or transferee) under the Exchange Act or other public announcement shall be required or shall be made voluntarily in connection with such transfer or distribution (other than a filing on a Form 5 made after the expiration of the lock-up period); (ii) transfer shares of common stock (A) as a bona fide gift, (B) to any trust for the direct or indirect benefit of such party or the immediate family member of such party, or if such party is a trust, to any beneficiary (including such beneficiary’s estate) of such party, (C) by will or intestate succession upon the death of such party, or (D) to another corporation, partnership, limited liability company, trust or other business entity that is a direct or indirect affiliate (as defined in Rule 405 promulgated under the Securities Act) of the party subject to the lock-up restrictions or as part of a distribution without consideration to stockholders, beneficiaries, partners, members or other equity holders, provided that in the case of any transfer contemplated in clauses (A) through (D) above, each donee, heir, distributee or other transferee shall execute and deliver a lock-up letter substantially in the form executed by the party subject to the lock-up restrictions, and provided, further, that no filing by any party (donor, donee, transferor or transferee) under the Exchange Act or other public announcement shall be required or shall be made voluntarily in connection with such transfer or distribution (other than a filing on a Form 5 made after the expiration of the lock-up period); (iii) exercise options to purchase common stock or settlement of restricted stock units pursuant to our equity incentive plans or of warrants to purchase our securities, or the exchange or conversion of any securities convertible or exchangeable for common stock granted pursuant to our equity incentive plans, in each case which equity incentive plans and warrants are described in this prospectus supplement, provided that any exercise or settlement does not involve a sale of securities to any person or entity other than us, whether to cover the applicable exercise price, withholding tax obligation or otherwise, provided, further, that the securities received upon such exercise, settlement, exchange or conversion shall be subject to the terms of this letter agreement and that no filing by any party under the Exchange Act or other public announcement shall be required or shall be made voluntarily in connection therewith (other than a filing on a Form 5 made after the expiration of the lock-up period); (iv) dispose shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock to us pursuant to agreements under which the shares were issued and we have the option to repurchase such shares or securities or a right of first refusal with

respect to transfers of such shares or securities, provided that no filing under Section 16(a) of the Exchange Act shall be required or shall be voluntarily made within 30 days after the date of this prospectus supplement, and after such 30th day, any filing under Section 16(a) of the Exchange Act shall clearly indicate in the footnotes thereto that (A) the filing relates to the transfer of such shares or securities to the Company pursuant to such repurchase option or right of first refusal, as the case may be, and (B) no shares were sold by the reporting person; (v) make transfers pursuant to a bona fide third-party tender offer, merger, consolidation or other similar transaction made to all holders of our capital stock involving a change of control of the Company, provided that in the event that such tender offer, merger, consolidation or other such transaction is not completed, the securities held by the party subject to the lock-up restrictions shall remain subject to such restrictions; (vi) transfer shares by operation of law, such as pursuant to a domestic relations order or in connection with a divorce settlement, provided that any transferee shall execute and deliver a lock-up letter substantially in the form executed by the party subject to the lock-up restrictions; (vii) establish a written plan meeting the requirements of Rule 10b5-1 under the Exchange Act relating to the sale of securities, provided that the securities subject to such plan may not be sold and no public disclosure of any such action shall be required or shall be voluntarily made by any person during the lock-up period; and (viii) sell or transfer shares of our common stock pursuant to a trading plan pursuant to Rule 10b5-1 that has been entered into by the party subject to the lock-up restrictions prior to the date of this prospectus supplement, provided, that to the extent a public announcement or filing under the Exchange Act, if any, is required or voluntarily made by or on behalf of the party subject to the lock-up restrictions or the Company regarding any such sales or transfers, such announcement or filing shall include a statement to the effect that the sale or transfer was made pursuant to a trading plan pursuant to Rule 10b5-1.

The lock-up provision will not restrict broker-dealers from engaging in market making and similar activities conducted in the ordinary course of their business.

Cowen and Company, LLC and Piper Sandler & Co., in their sole discretion, may release our common stock and other securities subject to the lock-up agreements described above in whole or in part at any time. When determining whether or not to release our common stock and other securities from lock-up agreements, Cowen and Company, LLC and Piper Sandler & Co. will consider, among other factors, the holder's reasons for requesting the release, the number of shares for which the release is being requested and market conditions at the time of the request.

Electronic Offer, Sale and Distribution of Shares. A prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters or selling group members, if any, participating in this offering and one or more of the underwriters participating in this offering may distribute prospectuses electronically. The representatives may agree to allocate a number of shares or pre-funded warrants to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters and selling group members that will make internet distributions on the same basis as other allocations. Other than the prospectus in electronic format, the information on these websites is not part of this prospectus or the registration statement of which this prospectus forms a part, has not been approved or endorsed by us or any underwriter in its capacity as underwriter, and should not be relied upon by investors.

Other Relationships. Certain of the underwriters and their affiliates have provided, and may in the future provide, various investment banking, commercial banking and other financial services for us and our affiliates for which they have received, and may in the future receive, customary fees. Cowen and Company, LLC and Piper Sandler & Co. also served as underwriters in our public offering in January 2016. We also entered into an "at the market" sales agreement with Cowen and Company, LLC, dated as of August 1, 2019, under which we may issue and sell from time to time up to $40.0 million of our common stock through Cowen and Company, LLC as our sales agent.

Selling Restrictions

Canada. The shares of common stock and pre-funded warrants may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the shares of common stock or pre-funded warrants must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

United Kingdom. In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are "qualified investors" (as defined in the Prospectus Regulation) (i) who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the "Order") and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons") or otherwise in circumstances which have not resulted and will not result in an offer to the public of the shares or pre-funded warrants in the United Kingdom within the meaning of the Financial Services and Markets Act 2000.

Any person in the United Kingdom that is not a relevant person should not act or rely on the information included in this document or use it as basis for taking any action. In the United Kingdom, any investment or investment activity that this document relates to may be made or taken exclusively by relevant persons.

European Economic Area and the UK. In relation to each member state of the European Economic Area and the United Kingdom, or each, a "Relevant State," no shares or pre-funded warrants have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the shares and pre-funded warrants which has been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation, except that offers of shares and pre-funded warrants may be made to the public in that Relevant State at any time under the following exemptions under the Prospectus Regulation:

A. to any legal entity which is a qualified investor as defined under the Prospectus Regulation;
B. to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation), subject to obtaining the prior consent of the underwriters; or
C. in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of shares and pre-funded warrants shall require the Company or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation and each person who initially acquires any shares or pre-funded warrants or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with each of the underwriters and the Company that it is a "qualified investor" within the meaning of Article 2(e) of the Prospectus Regulation. In the case of any shares or pre-funded warrants being offered to a financial intermediary as that term is used in the Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares or pre-funded warrants acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares or pre-funded warrants to the public other than their offer or resale in a Relevant State to qualified investors as so defined or in circumstances in which the prior consent of the underwriters have been obtained to each such proposed offer or resale.

For the purposes of this provision, the expression an "offer to the public" in relation to shares and pre-funded warrants in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares and pre-funded warrants to be offered so as to enable an investor to decide to purchase or subscribe for any shares, and the expression "Prospectus Regulation" means Regulation (EU) 2017/1129.

France. This prospectus supplement has not been prepared in the context of a public offering of financial securities in France within the meaning of Article L.411-1 of the French Code Monétaire et Financier and Title I of Book II of the Reglement Général of the Autorité des marchés financiers, or the AMF, and therefore has not been and will not be filed with the AMF for prior approval or submitted for clearance to the AMF. Consequently, the shares of our common stock and pre-funded warrants may not be, directly or indirectly, offered or sold to the public in France and offers and sales of the shares of our common stock or pre-funded warrants may only be made in France to qualified investors (investisseurs qualifiés) acting for their own, as defined in and in accordance with Articles L.411-2 and D.411-1 to D.411-4, D.734-1, D.744-1, D.754-1 and D.764-1 of the French Code Monétaire et Financier. Neither this prospectus supplement nor any other offering material may be released, issued or distributed to the public in France or used in connection with any offer for subscription on sale of the shares of our common stock or pre-funded warrants to the public in France. The subsequent direct or indirect retransfer of the shares of our common stock or pre-funded warrants to the public in France may only be made in compliance with Articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French Code Monétaire et Financier.

Germany. Each person who is in possession of this prospectus supplement is aware of the fact that no German securities prospectus (wertpapierprospekt) within the meaning of the securities prospectus act (wertpapier-prospektgesetz), or the act, of the federal republic of Germany has been or will be published with respect to the shares of our common stock and pre-funded warrants. In particular, each underwriter has represented that it has not engaged and has agreed that it will not engage in a public offering in the federal republic of Germany (ôffertliches angebot) within the meaning of the act with respect to any of the shares of our common stock or pre-funded warrants otherwise than in accordance with the act and all other applicable legal and regulatory requirements.

Switzerland. The shares common stock and pre-funded warrants may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document does not constitute a prospectus within the meaning of, and has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock

exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or pre-funded warrants or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company, the shares or pre-funded warrants have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares and pre-funded warrants will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA (FINMA), and the offer of shares and pre-funded warrants has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares or pre-funded warrants.

Netherlands. The offering of the shares of our common stock and pre-funded warrants is not a public offering in The Netherlands. The shares of our common stock or pre-funded warrants may not be offered or sold to individuals or legal entities in The Netherlands unless (1) a prospectus relating to the offer is available to the public, which has been approved by the Dutch Authority for the Financial Markets (Autoriteit Financiële Markten) or by the competent supervisory authority of another state that is a member of the European Union or party to the Agreement on the European Economic Area, as amended or (2) an exception or exemption applies to the offer pursuant to Article 5:3 of The Netherlands Financial Supervision Act (Wet op het financieel toezicht) or Article 53 paragraph 2 or 3 of the Exemption Regulation of the Financial Supervision Act, for instance due to the offer targeting exclusively “qualified investors” (gekwalificeerde beleggers) within the meaning of Article 1:1 of The Netherlands Financial Supervision Act.

Israel. In the State of Israel this prospectus supplement shall not be regarded as an offer to the public to purchase shares of common stock or pre-funded warrants under the Israeli Securities Law, 5728—1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728-1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions (the “Addressed Investors”); or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728—1968, subject to certain conditions (the “Qualified Investors”). The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. The company has not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728—1968. We have not and will not distribute this prospectus supplement or make, distribute or direct an offer to subscribe for our common stock or pre-funded warrants to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728—1968. In particular, we may request, as a condition to be offered common stock, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728—1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728—1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728—1968 and the regulations promulgated thereunder in connection with the offer to be issued common stock; (iv) that the shares of common stock and pre-funded warrants that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728—1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728—1968; and (v) that it is willing to

provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor's name, address and passport number or Israeli identification number.

Japan. The shares and pre-funded warrants have not been and will not be registered under the Financial Instruments and Exchange Act. Accordingly, the shares and pre-funded warrants may not be offered or sold, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to or for the benefit of a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Act and any other applicable laws, regulations and ministerial guidelines of Japan.

Hong Kong. The shares and pre-funded warrants have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to our common stock has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to our common stock which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

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

Where the shares or pre-funded warrants are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares or pre-funded warrants pursuant to an offer made under Section 275 of the SFA except:

- to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
- where no consideration is or will be given for the transfer;
- where the transfer is by operation of law;
- as specified in Section 276(7) of the SFA; or
- as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

We have not authorized and do not authorize the making of any offer of securities through any financial intermediary on our behalf, other than offers made by the underwriters and their respective affiliates, with a view to the final placement of the securities as contemplated in this document. Accordingly, no purchaser of the shares or pre-funded warrants, other than the underwriters, is authorized to make any further offer of shares on our behalf or on behalf of the underwriters.

LEGAL MATTERS

The validity of the securities offered by this prospectus supplement and accompanying prospectus will be passed upon by Wilson Sonsini Goodrich & Rosati, P.C., Palo Alto, California. Certain members of, and investment partnerships comprised of members of, and persons associated with, Wilson Sonsini Goodrich & Rosati, P.C., own an aggregate of 15,707 shares of our common stock. Cooley LLP, San Diego, California, is acting as counsel for the underwriters.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2019, and the effectiveness of our internal control over financial reporting as of December 31, 2019, as set forth in their reports, which are incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and other reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at www.sec.gov. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K, including any amendments to those reports, and other information that we file with or furnish to the SEC pursuant to Section 13(a) or 15(d) of the Exchange Act can also be accessed free of charge through the Internet. These filings will be available as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

We have filed with the SEC a registration statement under the Securities Act of 1933 relating to the offering of these securities. The registration statement, including the attached exhibits, contains additional relevant information about us and the securities. This prospectus supplement and the accompanying prospectus do not contain all of the information set forth in the registration statement. You can obtain a copy of the registration statement, at prescribed rates, from the SEC at the address listed above. The registration statement and the documents referred to below under "Information Incorporated by Reference" are also available on our Internet website, www.otonomy.com. We have not incorporated by reference into this prospectus supplement or the accompanying prospectus the information on our website, and you should not consider it to be a part of this prospectus supplement or the accompanying prospectus.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus supplement and the accompanying prospectus certain information we file with it, which means that we can disclose important information by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus supplement and the accompanying prospectus, and information that we file later with the SEC will automatically update and supersede information contained in this prospectus supplement and the accompanying prospectus. We incorporate by reference the documents listed below that we have previously filed with the SEC (excluding any portions of any Form 8-K that are not deemed "filed" pursuant to the General Instructions of Form 8-K):

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2019, filed with the SEC on February 27, 2020 (the Annual Report);
- the information specifically incorporated by reference into the Annual Report from our definitive proxy statement on Schedule 14A (filed with the SEC on April 27, 2020 and as supplemented on June 10, 2020);
- our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2020 (filed with the SEC on May 7, 2020);
- our Current Reports on Form 8-K filed with the SEC on January 9, 2020, February 27, 2020, April 9, 2020, May 7, 2020, June 26, 2020, July 6, 2020 and July 9, 2020; and
- the description of our common stock contained in our Registration Statement on Form 8-A as filed with the SEC on August 5, 2014 pursuant to Section 12(b) of the Exchange Act.

We also incorporate by reference into this prospectus supplement and accompanying prospectus additional documents (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits on such form that are related to such items) that we may file with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the completion or termination of the offering, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information deemed

furnished and not filed with the SEC. Any statements contained in a previously filed document incorporated by reference into this prospectus supplement and accompanying prospectus is deemed to be modified or superseded for purposes of this prospectus supplement and accompanying prospectus to the extent that a statement contained in this prospectus supplement or accompanying prospectus, or in a subsequently filed document also incorporated by reference herein, modifies or supersedes that statement.

This prospectus supplement and accompanying prospectus may contain information that updates, modifies or is contrary to information in one or more of the documents incorporated by reference in this prospectus supplement and accompanying prospectus. You should rely only on the information incorporated by reference or provided in this prospectus supplement and accompanying prospectus. We have not authorized anyone else to provide you with different information. You should not assume that the information in this prospectus supplement or accompanying prospectus is accurate as of any date other than the date of this prospectus supplement or accompanying prospectus, or the date of the documents incorporated by reference in this prospectus supplement and accompanying prospectus.

We will provide to each person, including any beneficial owner, to whom this prospectus supplement and accompanying prospectus is delivered, upon written or oral request, at no cost to the requester, a copy of any and all of the information that is incorporated by reference in this prospectus supplement and accompanying prospectus.

Requests for such documents should be directed to:

Otonomy, Inc.
4796 Executive Drive
San Diego, CA 92121
Attention: Secretary

You may also access the documents incorporated by reference in this prospectus supplement and accompanying prospectus through our website at www.otonomy.com. Except for the specific incorporated documents listed above, no information available on or through our website shall be deemed to be incorporated in this prospectus supplement and accompanying prospectus or the registration statement of which they forms a part.

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PROSPECTUS

$150,000,000

Otonomy, Inc.

By this prospectus, Otonomy may offer, from time to time:

- Common stock
- Preferred stock
- Depositary shares
- Warrants
- Debt securities
- Subscription Rights
- Units

All of the securities listed above may be sold separately or as units with other securities.

We may offer and sell from time to time, in one or more series or issuances and on terms that we will determine at the time of the offering, any combination of the securities described in this prospectus, either individually or as units comprising one or more of the other classes of securities, up to an aggregate amount of $150,000,000.

We will provide specific terms of any offering in a supplement to this prospectus. Any prospectus supplement may also add, update or change information contained in this prospectus. You should carefully read this prospectus and the applicable prospectus supplement as well as the documents incorporated or deemed to be incorporated by reference in this prospectus before you purchase any of the securities offered hereby.

These securities may be offered and sold in the same offering or in separate offerings; to or through underwriters, dealers and agents; or directly to purchasers. The names of any underwriters, dealers or agents involved in the sale of our securities, their compensation and any over-allotment options held by them will be described in the applicable prospectus supplement. See the section titled “Plan of Distribution.”

Our common stock is listed on The NASDAQ Global Select Market under the symbol “OTIC”. We will provide information in any applicable prospectus supplement regarding any listing of securities other than shares of our common stock on any securities exchange.

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.

INVESTING IN OUR SECURITIES INVOLVES SIGNIFICANT RISKS. YOU SHOULD REVIEW CAREFULLY THE “RISK FACTORS” ON PAGE 6 OF THIS PROSPECTUS AND IN THE APPLICABLE PROSPECTUS SUPPLEMENT BEFORE INVESTING IN OUR SECURITIES.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities, or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is September 21, 2018

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the United States Securities and Exchange Commission, or the SEC, using a “shelf” registration process. Under this shelf process, we may, from time to time, offer and sell any combination of the securities described in this prospectus in one or more offerings up to a total amount of $150,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add to, update or change information contained in the prospectus and, accordingly, to the extent inconsistent, information in this prospectus is superseded by the information in the prospectus supplement.

The prospectus supplement to be attached to the front of this prospectus may describe, as applicable: the terms of the securities offered; the initial price to the public; the price paid for the securities; net proceeds; and the other specific terms related to the offering of the securities.

You should only rely on the information contained or incorporated by reference in this prospectus and any prospectus supplement or free writing prospectus relating to a particular offering. No person has been authorized to give any information or make any representations in connection with this offering other than those contained or incorporated by reference in this prospectus, any accompanying prospectus supplement and any related free writing prospectus in connection with the offering described herein and therein, and, if given or made, such information or representations must not be relied upon as having been authorized by us. Neither this prospectus nor any prospectus supplement nor any related free writing prospectus shall constitute an offer to sell or a solicitation of an offer to buy offered securities in any jurisdiction in which it is unlawful for such person to make such an offering or solicitation. This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of the securities, you should refer to the registration statement, including its exhibits.

You should read the entire prospectus and any prospectus supplement and any related free writing prospectus, as well as the documents incorporated by reference into this prospectus or any prospectus supplement or any related free writing prospectus, before making an investment decision. Neither the delivery of this prospectus or any prospectus supplement or any free writing prospectus nor any sale made hereunder shall under any circumstances imply that the information contained or incorporated by reference herein or in any prospectus supplement or free writing prospectus is correct as of any date subsequent to the date hereof or of such prospectus supplement or free writing prospectus, as applicable. You should assume that the information appearing in this prospectus, any prospectus supplement or any document incorporated by reference is accurate only as of the date of the applicable documents, regardless of the time of delivery of this prospectus or any sale of securities. Our business, financial condition, results of operations and prospects may have changed since that date.

Prospectus Summary

This summary description about us and our business highlights selected information contained elsewhere in this prospectus or incorporated in this prospectus by reference. This summary does not contain all of the information you should consider before buying securities in this offering. You should carefully read this entire prospectus and any applicable prospectus supplement, including each of the documents incorporated herein or therein by reference, before making an investment decision. Unless the context otherwise requires, the terms "Otonomy," "the Company," "we," "us" and "our" in this prospectus refer to Otonomy, Inc., and its subsidiaries.

Otonomy, Inc.

Overview

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

OTIVIDEX™ is a steroid in development for the treatment of Ménière's disease. Two Phase 3 trials in Ménière's disease patients were completed in the second half of 2017. The AVERTS-2 trial, conducted in Europe, achieved its primary endpoint (p value = 0.029) while the AVERTS-1 trial, conducted in the United States, did not (p value = 0.62). Based on a Type C meeting with the FDA, we believe that one additional successful pivotal trial is sufficient to support the U.S. registration of OTIVIDEX in Ménière's disease, and recently announced the initiation of such trial. We expect top-line results from this trial in the first half of 2020.

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

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

In addition, we developed, received FDA approval for and commercially launched OTIPRIO® (ciprofloxacin otic suspension) for use during tympanostomy tube placement, or TTP, surgery in pediatric patients. OTIPRIO was also approved by the FDA for the treatment of acute otitis externa, or AOE. In November 2017, we announced the discontinuation of promotional support for OTIPRIO in order to significantly reduce operating expenses related to the product. The Company recently announced the initiation of a partnership with privately held Mission Pharmacal, or Mission, to support the promotion of OTIPRIO for the treatment of AOE in pediatric and primary care physician offices as well as urgent care clinics.

Corporate Information

We were incorporated in the State of Delaware in May 2008. Our principal executive offices are located at 4796 Executive Drive, San Diego, California 92121, and our telephone number is (619) 323-2200. 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.

Otonomy, the Otonomy logo, OTIPRIO, OTIVIDEX and other trademarks or service marks of Otonomy appearing in this report are the property of Otonomy. This prospectus and the documents incorporated by reference herein contain additional trade names, trademarks and service marks of other companies. We do not intend our use or display of other companies' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies. We have omitted the ® and ™ designations, as applicable, for the trademarks used in this prospectus.

Implications of Being an Emerging Growth Company

We qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. An emerging growth company may take advantage of relief from certain reporting requirements and other burdens that are otherwise applicable generally to public companies. As an emerging growth company:

- we have availed ourselves of the exemption from the requirement to obtain an attestation and report from our auditors on the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act of 2002;
- we will provide less extensive disclosure about our executive compensation arrangements; and
- we will not require shareholder non-binding advisory votes on executive compensation or golden parachute arrangements.

We may use these provisions until the last day of our fiscal year following the fifth anniversary of our initial public offering, or December 31, 2019. However, if certain events occur prior to the end of such five-year period, including if we become a "large accelerated filer," our annual gross revenues exceed $1.07 billion or we issue more than $1.0 billion of non-convertible debt in any three-year period, we will cease to be an emerging growth company prior to the end of such five-year period. We may choose to take advantage of some but not all of these reduced burdens. To the extent that we take advantage of these reduced burdens, the information that we provide stockholders may be different than you might obtain from other public companies in which you hold equity interests.

The Securities We May Offer

We may offer up to $150,000,000 of common stock, preferred stock, depositary shares, warrants, debt securities, subscription rights and units in one or more offerings and in any combination.

Common Stock

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders. Our amended and restated certificate of incorporation does not provide for cumulative voting rights. Subject to preferences that may apply to any shares of preferred stock outstanding at the time, the holders of our common stock are entitled to receive dividends out of funds legally available if our board of directors, in its discretion, determines to issue dividends and then only at the times and in the amounts that our board of

directors may determine. If we become subject to a liquidation, dissolution or winding-up, the assets legally available for distribution to our stockholders would be distributable ratably among the holders of our common stock and any participating preferred stock outstanding at that time, subject to prior satisfaction of all outstanding debt and liabilities and the preferential rights of and the payment of liquidation preferences, if any, on any outstanding shares of preferred stock.

Preferred Stock and Depositary Shares

Our board of directors has the authority, subject to limitations prescribed by Delaware law, to issue preferred stock in one or more series, to establish from time to time the number of shares to be included in each series, and to fix the designation, powers, preferences and rights of the shares of each series and any of its qualifications, limitations or restrictions, in each case without further vote or action by our stockholders.

We may also issue fractional shares of preferred stock that will be represented by depositary shares and depositary receipts.

Each series of preferred stock, depositary shares or depositary receipts, if issued, will be more fully described in the particular prospectus supplement that will accompany this prospectus, including redemption provisions, rights in the event of our liquidation, dissolution or winding-up, voting rights and rights to convert into common stock. We have no present plans to issue any shares of preferred stock, depositary shares or depositary receipts nor are any shares of our preferred stock, depositary shares or depositary receipts presently outstanding.

Warrants

We may issue warrants for the purchase of common stock, preferred stock or debt securities. We may issue warrants independently or together with other securities.

Debt Securities

We may offer secured or unsecured obligations in the form of one or more series of senior or subordinated debt. The senior debt securities and the subordinated debt securities are together referred to in this prospectus as the “debt securities.” The subordinated debt securities generally will be entitled to payment only after payment of our senior debt. Senior debt generally includes all debt for money borrowed by us, except debt that is stated in the instrument governing the terms of that debt to be not senior to, or to have the same rank in right of payment as, or to be expressly junior to, the subordinated debt securities. We may issue debt securities that are convertible into shares of our common stock.

The senior and subordinated debt securities will be issued under separate indentures between us and a trustee. We have summarized the general features of the debt securities to be governed by the indentures. These indentures have been filed as exhibits to the registration statement of which this prospectus forms a part. We encourage you to read these indentures. Instructions on how you can get copies of these documents are provided in the section titled “Where You Can Find More Information.”

Subscription Rights

We may issue subscription rights to purchase our common stock, preferred stock or debt securities. These subscription rights may be offered independently or together with any other security offered hereby and may or may not be transferable by the stockholder receiving the subscription rights in such offering.

Units

We may issue units comprising one or more of the other classes of securities issued by us as described in this prospectus in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit.

RISK FACTORS

An investment in our securities involves a high degree of risk. The prospectus supplement applicable to each offering of our securities will contain a discussion of the risks applicable to an investment in our securities. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed in the section titled "Risk Factors" in the applicable prospectus supplement, together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. You should also consider the risks, uncertainties and assumptions discussed under "Part I—Item 1A—Risk Factors" in our most recent Annual Report on Form 10-K and "Part II—Item 1A—Risk Factors" in our Quarterly Reports on Form 10-Q, all of which are incorporated herein by reference, and as may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future and any prospectus supplement related to a particular offering. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations.

FORWARD-LOOKING STATEMENTS

This prospectus, each prospectus supplement and the information incorporated by reference in this prospectus and each prospectus supplement contain certain statements that constitute "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act.

Our forward-looking statements include, but are not limited to, statements about:

- our expectations regarding our OTIPRIO promotional partnership;
- our expectations regarding our clinical development of OTIVIDEX, including availability of top-line results from the recently initiated additional Phase 3 trial in the first half of 2020;
- our expectations regarding the clinical development of OTO-313, including but not limited to our plans to initiate a Phase 1/2 clinical trial in tinnitus patients in the first half of 2019;
- our expectations regarding the clinical development of OTO-413, including but not limited to our plans to initiate a Phase 1/2 clinical trial in hearing loss patients in the first half of 2019;
- the timing or likelihood of regulatory filings and approvals;
- our expectations regarding the future development of other product candidates, including but not limited to our plans to select a candidate for clinical development for both the OTO-5XX and OTO-6XX programs by the end of 2018;
- the potential for commercialization of our product candidates, if approved;
- our expectations and statements regarding the pricing, market size, opportunity and growth potential for OTIVIDEX, OTO-313, OTO-413 and our other product candidates, if approved for commercial use;
- our expectations and statements regarding the adoption and use of OTIPRIO and OTIVIDEX, OTO-313 and OTO-413, if approved;
- our expectations regarding potential coverage and reimbursement relating to OTIPRIO, and OTIVIDEX, OTO-313 and OTO-413, if approved, or any other approved product candidates;
- our plans regarding the use of contract manufacturers for the production of our product candidates for clinical trials and, if approved, commercial use;
- our plans and ability to effectively establish and manage our own sales and marketing capabilities, or seek and establish collaborative partners, to commercialize our products;

- our ability to advance product candidates into, and successfully complete, clinical trials;
- the implementation of our business model, strategic plans for our business, products and technology;
- the initiation, timing, progress and results of future nonclinical studies and clinical trials;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our products and technology;
- estimates of our expenses, future revenue, capital requirements and our needs for additional financing;
- our financial performance;
- accounting principles, policies and estimates;
- developments and projections relating to our competitors and our industry; and
- our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act.

These forward-looking statements are subject to a number of risks, uncertainties, and assumptions, including but not limited to: our limited operating history and our expectation that we will incur significant losses for the foreseeable future; our ability to obtain additional financing; our dependence on the commercial success of OTIPRIO and the regulatory success and advancement of additional product candidates, including but not limited to OTIVIDEX, OTO-313, and OTO-413; the uncertainties inherent in the clinical drug development process, including, without limitation, our ability to adequately demonstrate the safety and efficacy of our product candidates, the nonclinical and clinical results for our product candidates, which may not support further development, and challenges related to patient enrollment in clinical trials; our ability to obtain regulatory approval for our product candidates; side effects or adverse events associated with our product candidates; competition in the biopharmaceutical industry; our dependence on third parties to conduct nonclinical studies and clinical trials; the timing and outcome of hospital pharmacy and therapeutics reviews and other facility reviews; the impact of coverage and reimbursement decisions by third-party payors on the pricing and market acceptance of OTIPRIO; our dependence on third parties for the manufacture of OTIPRIO and product candidates; our dependence on a small number of suppliers for raw materials; our ability to protect our intellectual property related to OTIPRIO and our product candidates in the United States and throughout the world; expectations regarding potential market size, opportunity and growth; our ability to manage operating expenses; implementation of our business model and strategic plans for our business, products and technology; and other risks.

The words “believe,” “may,” “will,” “potentially,” “estimate,” “continue,” “anticipate,” “intend,” “could,” “would,” “project,” “plan,” “goal,” “expect” and the negative and plural forms of these words and similar expressions are intended to identify forward-looking statements, but are not the exclusive means of identifying such statements. Those statements appear in this prospectus, any accompanying prospectus supplement and the documents incorporated herein and therein by reference, particularly in the sections titled “Prospectus Summary,” “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Business,” and include statements regarding the intent, belief or current expectations of the Company and management that are subject to known and unknown risks, uncertainties and assumptions.

This prospectus, any prospectus supplement and the information incorporated by reference in this prospectus and any prospectus supplement also contain statements that are based on the current expectations of our Company and management. You are cautioned that any such forward-looking statements are not guarantees of future performance and involve risks and uncertainties, and that actual results may differ materially from those projected in the forward-looking statements as a result of various factors.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus,

and although we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted a thorough inquiry into, or review of, all potentially available relevant information.

Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not unduly rely upon forward-looking statements as predictions of future events. The events and circumstances reflected in the forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Except as required by applicable law, including the securities laws of the United States and the rules and regulations of the SEC, we do not plan to publicly update or revise any forward-looking statements contained herein after we distribute this prospectus, whether as a result of any new information, future events or otherwise.

RATIO OF EARNINGS TO FIXED CHARGES

The following table sets forth our ratio of earnings to fixed charges for each of the periods indicated. You should read these ratios in connection with our annual report on Form 10-K for the period ended December 31, 2017 (including our financial statements and accompanying notes contained therein) incorporated by reference in this prospectus, and our quarterly report on Form 10-Q for the period ended June 30, 2018, incorporated by reference in this prospectus.

	Six Months Ended	Year Ended December 31,		
	June 30, 2018	2017	2016	2015
Ratio of earnings to fixed charges	N/A	N/A	N/A	N/A

The ratio of earnings to fixed charges represents the number of times that fixed charges are covered by earnings. Earnings consist of loss from continuing operations before income taxes and fixed charges. Fixed charges consist of estimated interest expense within rental expense.

We did not record positive earnings for the periods indicated in the table above. Accordingly, our earnings were insufficient to cover fixed charges for such periods and we are unable to disclose a ratio of earnings to fixed charges for such periods. For the six months ended June 30, 2018 and the years ended December 31, 2017, 2016, and 2015, the coverage deficiency necessary for the ratio of earnings to fixed charges to equal 1.00 (one-to-one coverage) was $25.0 million, $90.1 million, $110.6 million, and $61.7 million, respectively, for each of such periods.

As of the date of this prospectus, we have no shares of preferred stock outstanding, and consequently, our ratio of earnings to combined fixed charges and preferred share dividends and ratio of earnings to fixed charges would be identical.

USE OF PROCEEDS

Unless otherwise indicated in a prospectus supplement, we will use the net proceeds from the sale of securities offered by this prospectus for general corporate purposes, which may include working capital, capital expenditures, other corporate expenses and acquisitions of complementary products, technologies or businesses. However, we do not have agreements or commitments for any specific acquisitions at this time. The timing and amount of our actual expenditures will be based on many factors, including cash flows from operations and the anticipated growth of our business, the progress of our development and commercialization efforts and the status and results of our clinical trials, as well as any collaborations that we may enter into with third parties and any unforeseen cash needs. As a result, unless otherwise indicated in the prospectus supplement, our management will have broad discretion to allocate the net proceeds of the offerings. Pending their ultimate use, we intend to invest the net proceeds in short-term, investment-grade, interest-bearing instruments.

DESCRIPTION OF CAPITAL STOCK

General

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

Common Stock

Outstanding Shares

As of June 30, 2018, there were 30,630,125 shares of common stock outstanding. Our board of directors is authorized, without stockholder approval, to issue additional shares of our capital stock.

As of June 30, 2018, there were 5,146,089 shares of common stock subject to outstanding options.

Dividend Rights and Policy

Subject to preferences that may be applicable to any then outstanding convertible preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

We have never declared or paid cash dividends on any of our capital stock. We currently intend to retain all available funds and any future earnings, if any, for the operation and expansion of our business and, therefore, we do not anticipate declaring or paying cash dividends in the foreseeable future. In addition, we may become subject to covenants under future debt arrangements that place restrictions on our ability to pay dividends. The payment of dividends, if any, will be at the discretion of our board of directors and will depend on our results of operations, capital requirements, financial condition, prospects, contractual arrangements, any limitations on payment of dividends present in our future debt agreements, and other factors that our board of directors may deem relevant.

Voting Rights

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

Right to Receive Liquidation Distributions

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

Rights and Preferences

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

Fully Paid and Nonassessable

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

Preferred Stock

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

Stock Options

As of June 30, 2018, there were approximately 5,146,089 shares of our common stock issuable upon exercise of outstanding stock options, at a weighted-average exercise price of $5.79 per share.

Employee Stock Purchase Plan

As of June 30, 2018, 1,698,108 shares of our common stock were available for sale under our 2014 Employee Stock Purchase Plan.

Exclusive Jurisdiction

Unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware is the sole and exclusive forum for: (1) any derivative action or proceeding brought on behalf of us; (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders; (3) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law or our amended and restated certificate of incorporation or amended and restated bylaws; (4) any action asserting a claim against us governed by the internal affairs doctrine. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any action, a court could find the choice of forum provisions contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in such action.

Registration Rights

The holders of an aggregate of up to 4,192,638 shares of our common stock, including shares of common stock issuable upon the exercise of outstanding options and warrants, or their permitted transferees, are entitled to rights with respect to the registration of such shares under the Securities Act. We refer to these shares as "registrable securities." These rights are provided under the terms of our third amended and restated investors' rights agreement between us and the holders of registrable securities, and include demand registration rights, "piggyback" registration rights and Form S-3 registration rights.

These registration rights will terminate as to a given holder of registrable securities upon the earliest of (1) August 18, 2019 or (2) when such holder and such holder's affiliates can sell all of such holder's registrable securities during a three-month period without registration in compliance with Rule 144 of the Securities Act.

Generally, we are required to pay the registration expenses (other than underwriters' and brokers' discounts and commissions) in connection with the registrations described below, including the reasonable fees and disbursements of one counsel for the selling holder or holders of registrable securities. In an underwritten offering, the underwriters have the right to limit the number of shares registered by the holders of registrable securities for marketing reasons, subject to certain limitations.

Demand Registration Rights

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

Piggyback Registration Rights

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

Form S-3 Registration Rights

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

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

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

Delaware Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law regulating corporate takeovers. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging, under certain circumstances, in a business combination with an interested stockholder for a period of three years following the date the person became an interested stockholder unless:

- prior to the date of the transaction, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, but not for determining the outstanding voting stock owned by the interested stockholder, (1) voting stock owned by persons who are directors and also officers, and (2) voting stock owned by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- at or subsequent to the date of the transaction, the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock which is not owned by the interested stockholder.

Generally, a business combination includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of a corporation's outstanding voting stock. These provisions may have the effect of delaying, deferring or preventing a change in our control.

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

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

- *Board of directors vacancies*. Our amended and restated certificate of incorporation and amended and restated bylaws authorize only our board of directors to fill vacant directorships, including newly created seats. In addition, the number of directors constituting our board of directors is permitted to be set only by a resolution adopted by our board of directors. These provisions prevent a stockholder from increasing the size of our board of directors and then gaining control of our board of directors by filling the resulting vacancies with its own nominees. This makes it more difficult to change the composition of our board of directors but promotes continuity of management.
- *Classified board*. Our amended and restated certificate of incorporation and amended and restated bylaws provide that our board is classified into three classes of directors. A third party may be

discouraged from making a tender offer or otherwise attempting to obtain control of us as it is more difficult and time consuming for stockholders to replace a majority of the directors on a classified board of directors.

- *Stockholder action; special meeting of stockholders*. Our amended and restated certificate of incorporation provides that our stockholders may not take action by written consent, but may only take action at annual or special meetings of our stockholders. As a result, a holder controlling a majority of our capital stock is not be able to amend our amended and restated bylaws or remove directors without holding a meeting of our stockholders called in accordance with our amended and restated bylaws. Our amended and restated certificate of incorporation and amended and restated bylaws further provide that special meetings of our stockholders may be called only by a majority of our board of directors, the Chairman of our Board of Directors, our Chief Executive Officer or our President (in the absence of a Chief Executive Officer), thus prohibiting a stockholder from calling a special meeting. These provisions might delay the ability of our stockholders to force consideration of a proposal or for stockholders controlling a majority of our capital stock to take any action, including the removal of directors.
- *Advance notice requirements for stockholder proposals and director nominations*. Our amended and restated bylaws provide advance notice procedures for stockholders seeking to bring business before our annual meeting of stockholders or to nominate candidates for election as directors at our annual meeting of stockholders. Our amended and restated bylaws also specify certain requirements regarding the form and content of a stockholder's notice. These provisions might preclude our stockholders from bringing matters before our annual meeting of stockholders or from making nominations for directors at our annual meeting of stockholders if the proper procedures are not followed. We expect that these provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.
- *No cumulative voting*. The Delaware General Corporation Law provides that stockholders are not entitled to the right to cumulate votes in the election of directors unless a corporation's certificate of incorporation provides otherwise. Our amended and restated certificate of incorporation does not provide for cumulative voting.
- *Directors removed only for cause*. Our amended and restated certificate of incorporation provides that stockholders may remove directors only for cause.
- *Amendment of charter provisions*. Any amendment of the above provisions in our amended and restated certificate of incorporation would require approval by a majority of our board of directors and the holders of at least two-thirds of our then outstanding voting securities.
- *Issuance of undesignated preferred stock*. Our board of directors will have the authority, without further action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with rights and preferences, including voting rights, designated from time to time by our board of directors. The existence of authorized but unissued shares of preferred stock would enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or other means.

Transfer Agent and Registrar

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

Market Listing

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

DESCRIPTION OF THE DEPOSITARY SHARES

General

At our option, we may elect to offer fractional shares of preferred stock, rather than full shares of preferred stock. If we do elect to offer fractional shares of preferred stock, we will issue receipts for depositary shares and each of these depositary shares will represent a fraction of a share of a particular series of preferred stock, as specified in the applicable prospectus supplement. Each owner of a depositary share will be entitled, in proportion to the applicable fractional interest in shares of preferred stock underlying that depositary share, to all rights and preferences of the preferred stock underlying that depositary share. These rights may include dividend, voting, redemption and liquidation rights.

The shares of preferred stock underlying the depositary shares will be deposited with a bank or trust company selected by us to act as depositary, under a deposit agreement by and among us, the depositary and the holders of the depositary receipts. The depositary will be the transfer agent, registrar and dividend disbursing agent for the depositary shares.

The depositary shares will be evidenced by depositary receipts issued pursuant to the depositary agreement. Holders of depositary receipts agree to be bound by the deposit agreement, which requires holders to take certain actions such as filing proof of residence and paying certain charges.

The summary of terms of the depositary shares contained in this prospectus is not complete, and is subject to modification in any prospectus supplement for any issuance of depositary shares. You should refer to the forms of the deposit agreement, our amended and restated certificate of incorporation and the certificate of designation that are, or will be, filed with the SEC for the applicable series of preferred stock. The prospectus supplement relating to a particular issue of depositary shares will include, if applicable, a discussion of material U.S. federal income tax considerations.

Dividends

The depositary will distribute cash dividends or other cash distributions, if any, received in respect of the series of preferred stock underlying the depositary shares to the record holders of depositary receipts in proportion to the number of depositary shares owned by those holders on the relevant record date. The relevant record date for depositary shares will be the same date as the record date for the preferred stock.

In the event of a distribution other than in cash, the depositary will distribute property received by it to the record holders of depositary receipts that are entitled to receive the distribution, unless the depositary determines that it is not feasible to make the distribution. If this occurs, the depositary, with our approval, may adopt another method for the distribution, including selling the property and distributing the net proceeds to the holders.

Liquidation Preference

If a series of preferred stock underlying the depositary shares has a liquidation preference, in the event of our voluntary or involuntary liquidation, dissolution or winding up, holders of depositary shares will be entitled to receive the fraction of the liquidation preference accorded each share of the applicable series of preferred stock, as set forth in the applicable prospectus supplement.

Redemption

If a series of preferred stock underlying the depositary shares is subject to redemption, the depositary shares will be redeemed from the proceeds received by the depositary resulting from the redemption, in whole or in part, of the preferred stock held by the depositary. Whenever we redeem any preferred stock held by the depositary,

the depositary will redeem, as of the same redemption date, the number of depositary shares representing the preferred stock so redeemed. The depositary will mail the notice of redemption to the record holders of the depositary receipts promptly upon receiving the notice from us and not fewer than 20 or more than 60 days, unless otherwise provided in the applicable prospectus supplement, prior to the date fixed for redemption of the preferred stock.

Voting

Upon receipt of notice of any meeting at which the holders of preferred stock are entitled to vote, the depositary will mail the information contained in the notice of meeting to the record holders of the depositary receipts underlying the preferred stock. Each record holder of those depositary receipts on the record date will be entitled to instruct the depositary as to the exercise of the voting rights pertaining to the amount of preferred stock underlying that holder's depositary shares. The record date for the depositary will be the same date as the record date for the preferred stock. The depositary will, to the extent practicable, vote the preferred stock underlying the depositary shares in accordance with these instructions. We will agree to take all action that may be deemed necessary by the depositary in order to enable the depositary to vote the preferred stock in accordance with these instructions. The depositary will not vote the preferred stock to the extent that it does not receive specific instructions from the holders of depositary receipts.

Withdrawal of Preferred Stock

Owners of depositary shares will be entitled to receive upon surrender of depositary receipts at the principal office of the depositary and payment of any unpaid amount due to the depositary, the number of whole shares of preferred stock underlying their depositary shares.

Partial shares of preferred stock will not be issued. Holders of preferred stock will not be entitled to deposit the shares under the deposit agreement or to receive depositary receipts evidencing depositary shares for the preferred stock.

Amendment and Termination of the Deposit Agreement

The form of depositary receipt evidencing the depositary shares and any provision of the deposit agreement may be amended by agreement between the depositary and us. However, any amendment which materially and adversely alters the rights of the holders of depositary shares, other than fee changes, will not be effective unless the amendment has been approved by at least a majority of the outstanding depositary shares. The deposit agreement may be terminated by the depositary or us only if:

- all outstanding depositary shares have been redeemed; or
- there has been a final distribution of the preferred stock in connection with our dissolution and such distribution has been made to all the holders of depositary shares.

Charges of Depositary

We will pay all transfer and other taxes and governmental charges arising solely from the existence of the depositary arrangement. We will also pay charges of the depositary in connection with:

- the initial deposit of the preferred stock;
- the initial issuance of the depositary shares;
- any redemption of the preferred stock; and
- all withdrawals of preferred stock by owners of depositary shares.

Holders of depositary receipts will pay transfer, income and other taxes and governmental charges and other specified charges as provided in the deposit agreement for their accounts. If these charges have not been paid, the depositary may:

- refuse to transfer depositary shares;
- withhold dividends and distributions; and
- sell the depositary shares evidenced by the depositary receipt.

Miscellaneous

The depositary will forward to the holders of depositary receipts all reports and communications we deliver to the depositary that we are required to furnish to the holders of the preferred stock. In addition, the depositary will make available for inspection by holders of depositary receipts at the principal office of the depositary, and at such other places as it may from time to time deem advisable, any reports and communications we deliver to the depositary as the holder of preferred stock.

Neither the depositary nor we will be liable if either the depositary or we are prevented or delayed by law or any circumstance beyond the control of either the depositary or us in performing our respective obligations under the deposit agreement. Our obligations and the depositary's obligations will be limited to the performance in good faith of our or the depositary's respective duties under the deposit agreement. Neither the depositary nor we will be obligated to prosecute or defend any legal proceeding in respect of any depositary shares or preferred stock unless satisfactory indemnity is furnished. The depositary and we may rely on:

- written advice of counsel or accountants;
- information provided by holders of depositary receipts or other persons believed in good faith to be competent to give such information; and
- documents believed to be genuine and to have been signed or presented by the proper party or parties.

Resignation and Removal of Depositary

The depositary may resign at any time by delivering a notice to us. We may remove the depositary at any time. Any such resignation or removal will take effect upon the appointment of a successor depositary and its acceptance of such appointment. The successor depositary must be appointed within 60 days after delivery of the notice for resignation or removal. The successor depositary must be a bank and trust company having its principal office in the United States of America and having a combined capital and surplus of at least $50,000,000.

DESCRIPTION OF THE WARRANTS

General

We may issue warrants for the purchase of our debt securities, preferred stock or common stock, or any combination thereof. Warrants may be issued independently or together with our debt securities, preferred stock or common stock and may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and a bank or trust company, as warrant agent. The warrant agent will act solely as our agent in connection with the warrants. The warrant agent will not have any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants. This summary of certain provisions of the warrants is not complete. For the terms of a particular series of warrants, you should refer to the prospectus supplement for that series of warrants and the warrant agreement for that particular series.

Debt Warrants

The prospectus supplement relating to a particular issue of warrants to purchase debt securities will describe the terms of the debt warrants, including the following:

- the title of the debt warrants;
- the offering price for the debt warrants, if any;
- the aggregate number of the debt warrants;
- the designation and terms of the debt securities, including any conversion rights, purchasable upon exercise of the debt warrants;
- if applicable, the date from and after which the debt warrants and any debt securities issued with them will be separately transferable;
- the principal amount of debt securities that may be purchased upon exercise of a debt warrant and the exercise price for the warrants, which may be payable in cash, securities or other property;
- the dates on which the right to exercise the debt warrants will commence and expire;
- if applicable, the minimum or maximum amount of the debt warrants that may be exercised at any one time;
- whether the debt warrants represented by the debt warrant certificates or debt securities that may be issued upon exercise of the debt warrants will be issued in registered or bearer form;
- information with respect to book-entry procedures, if any; the currency or currency units in which the offering price, if any, and the exercise price are payable;
- if applicable, a discussion of material U.S. federal income tax considerations;
- the antidilution provisions of the debt warrants, if any;
- the redemption or call provisions, if any, applicable to the debt warrants;
- any provisions with respect to the holder’s right to require us to repurchase the warrants upon a change in control or similar event; and
- any additional terms of the debt warrants, including procedures, and limitations relating to the exchange, exercise and settlement of the debt warrants.

Debt warrant certificates will be exchangeable for new debt warrant certificates of different denominations. Debt warrants may be exercised at the corporate trust office of the warrant agent or any other office indicated in the prospectus supplement. Prior to the exercise of their debt warrants, holders of debt warrants will not have any of the rights of holders of the debt securities purchasable upon exercise and will not be entitled to payment of principal or any premium, if any, or interest on the debt securities purchasable upon exercise.

Equity Warrants

The prospectus supplement relating to a particular series of warrants to purchase our common stock or preferred stock will describe the terms of the warrants, including the following:

- the title of the warrants;
- the offering price for the warrants, if any;
- the aggregate number of warrants;
- the designation and terms of the common stock or preferred stock that may be purchased upon exercise of the warrants;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each security;
- if applicable, the date from and after which the warrants and any securities issued with the warrants will be separately transferable;
- the number of shares of common stock or preferred stock that may be purchased upon exercise of a warrant and the exercise price for the warrants;
- the dates on which the right to exercise the warrants shall commence and expire;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- if applicable, a discussion of material U.S. federal income tax considerations;
- the antidilution provisions of the warrants, if any;
- the redemption or call provisions, if any, applicable to the warrants;
- any provisions with respect to the holder's right to require us to repurchase the warrants upon a change in control or similar event; and
- any additional terms of the warrants, including procedures, and limitations relating to the exchange, exercise and settlement of the warrants.

Holders of equity warrants will not be entitled:

- to vote, consent or receive dividends;
- receive notice as stockholders with respect to any meeting of stockholders for the election of our directors or any other matter; or
- exercise any rights as stockholders of us.

The descriptions of the warrants in this prospectus and in any prospectus supplement are summaries of the material provisions of the applicable warrants. These descriptions do not restate those warrants in their entirety and may not contain all the information that you may find useful. We urge you to read the applicable warrants because they, and not the summaries, define your rights as holders of the warrants. For more information, please review the forms of the relevant warrants, which will be filed with the SEC promptly after the offering of warrants and will be available as described in the section titled "Where You Can Find More Information."

DESCRIPTION OF THE DEBT SECURITIES

The debt securities may be either secured or unsecured and will either be our senior debt securities or our subordinated debt securities. The debt securities will be issued under one or more separate indentures between us and a trustee to be specified in an accompanying prospectus supplement. Senior debt securities will be issued under a senior indenture and subordinated debt securities will be issued under a subordinated indenture. Together, the senior indenture and the subordinated indenture are called indentures in this description. This prospectus, together with the applicable prospectus supplement, will describe the terms of a particular series of debt securities.

The following is a summary of selected provisions and definitions of the indentures and debt securities to which any prospectus supplement may relate. The summary of selected provisions of the indentures and the debt securities appearing below is not complete and is subject to, and qualified entirely by reference to, all of the provisions of the applicable indenture and certificates evidencing the applicable debt securities. For additional information, you should look at the applicable indenture and the certificate evidencing the applicable debt security that is filed as an exhibit to the registration statement that includes the prospectus. In this description of the debt securities, the words “we,” “us,” or “our” refer only to Otonomy, Inc. and not to any of our subsidiaries, unless we expressly state or the context otherwise requires.

The following description sets forth selected general terms and provisions of the applicable indenture and debt securities to which any prospectus supplement may relate. Other specific terms of the applicable indenture and debt securities will be described in the applicable prospectus supplement. If any particular terms of the indenture or debt securities described in a prospectus supplement differ from any of the terms described below, then the terms described below will be deemed to have been superseded by that prospectus supplement.

General

Debt securities may be issued in separate series without limitation as to aggregate principal amount. We may specify a maximum aggregate principal amount for the debt securities of any series.

We are not limited as to the amount of debt securities we may issue under the indentures. Unless otherwise provided in a prospectus supplement, a series of debt securities may be reopened to issue additional debt securities of such series.

The prospectus supplement relating to a particular series of debt securities will set forth:

- whether the debt securities are senior or subordinated;
- the offering price;
- the title;
- any limit on the aggregate principal amount;
- the person who shall be entitled to receive interest, if other than the record holder on the record date;
- the date or dates the principal will be payable;
- the interest rate or rates, which may be fixed or variable, if any, the date from which interest will accrue, the interest payment dates and the regular record dates, or the method for calculating the dates and rates;
- the place where payments may be made;
- any redemption provisions at our option and any applicable redemption prices associated with these provisions;

- any obligation by us to redeem or repurchase any debt securities pursuant to any sinking fund or similar provision or any redemption or repurchase at the option of the holder and any applicable redemption or repurchase terms and conditions and prices associated with these provisions;
- if issued other than in denominations of U.S. $1,000 or any multiple of U.S. $1,000, the denominations in which the debt securities shall be issuable;
- if applicable, the method for determining how the principal, premium, if any, or interest will be calculated by reference to an index or formula;
- if other than U.S. currency, the currency or currency units in which principal, premium, if any, or interest will be payable and whether we or a holder may elect payment to be made in a different currency;
- if the principal, premium or interest on debt securities is payable at our option or the holder thereof in one or more currencies or currency units other than those in which debt securities are payable, the currency or currency units in which the principal, premium or interest on the debt securities as to which such election is made shall be payable on the terms and conditions associated with these provisions;
- the percentage of the principal amount at which the debt securities may be issued, and if other than the entire amount, the portion of the principal amount that will be payable upon acceleration of maturity;
- if the principal amount payable at stated maturity will not be determinable as of any date prior to stated maturity, the amount or method for determining the amount which will be deemed to be the principal amount;
- if applicable, whether the debt securities shall be subject to the defeasance provisions described below under “Satisfaction and Discharge; Defeasance” or such other defeasance provisions specified in the applicable prospectus supplement for the debt securities;
- any conversion or exchange provisions;
- whether the debt securities will be issuable in the form of a global security, the depositary for any such global security, the form of legends for any global security and the terms for exchanging any such global security into a definitive registered debt security;
- the deletion, addition or change in any event of default, and any change in the right of the trustee or the requisite percentage of holders to declare the principal amount due and payable;
- any change or modification to the subordination provisions applicable to the subordinated debt securities if different from those described below under “Subordinated Debt Securities;”
- any deletion, addition or change in the covenants set forth in Article 10 of the indentures;
- any paying agents, authenticating agents, security registrars or other agents for the debt securities, if other than the trustee;
- any provisions relating to any security provided for the debt securities, including any provisions regarding the circumstances under which collateral may be released or substituted;
- any provisions relating to guaranties for the securities and any circumstances under which there may be additional obligors;
- any provisions granting special rights to holders when a specified event occurs;
- any provision with respect to any special interest premium or other premium;
- any special tax provisions that apply to the debt securities;
- with respect to the debt securities that do not bear interest, the dates for certain required reports to the applicable trustee;

- any and all additional, eliminated or changed terms that will apply to the debt securities; and
- any other terms of such debt securities.

Unless otherwise specified in the prospectus supplement, the debt securities will be registered debt securities. Debt securities may be sold at a substantial discount below their stated principal amount, bearing no interest or interest at a rate which at time of issuance is below market rates. The U.S. federal income tax considerations applicable to debt securities sold at a discount will be described in the applicable prospectus supplement.

Exchange and Transfer

Debt securities may be transferred or exchanged at the office of the security registrar or at the office of any transfer agent designated by us.

We will not impose a service charge for any transfer or exchange, but we may require holders to pay any tax or other governmental charges associated with any transfer or exchange.

In the event of any partial redemption of debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange, any debt security of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt security of that series selected for redemption, in whole or in part, except the unredeemed portion of the debt security being redeemed in part.

We will appoint the trustee as the initial security registrar. Any transfer agent, in addition to the security registrar initially designated by us, will be named in the prospectus supplement. We may designate additional transfer agents or change transfer agents or change the office of the transfer agent. However, we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

Global Securities

The debt securities of any series may be represented, in whole or in part, by one or more global securities. Each global security will:

- be registered in the name of a depositary, or its nominee, that we will identify in a prospectus supplement;
- be deposited with the depositary or nominee or custodian; and
- bear any required legends.

No global security may be exchanged in whole or in part for debt securities registered in the name of any person other than the depositary or any nominee unless:

- the depositary has notified us that it is unwilling or unable to continue as depositary or has ceased to be qualified to act as depositary;
- an event of default is continuing with respect to the debt securities of the applicable series; or
- any other circumstance described in a prospectus supplement has occurred permitting or requiring the issuance of any such security.

As long as the depositary, or its nominee, is the registered owner of a global security, the depositary or nominee will be considered the sole owner and holder of the debt securities represented by the global security for

all purposes under the indentures. Except in the above limited circumstances, owners of beneficial interests in a global security will not be:

- entitled to have the debt securities registered in their names;
- entitled to physical delivery of certificated debt securities; or
- considered to be holders of those debt securities under the indenture.

Payments on a global security will be made to the depositary or its nominee as the holder of the global security. Some jurisdictions have laws that require that certain purchasers of securities take physical delivery of such securities in definitive form. These laws may impair the ability to transfer beneficial interests in a global security.

Institutions that have accounts with the depositary or its nominee are referred to as "participants." Ownership of beneficial interests in a global security will be limited to participants and to persons that may hold beneficial interests through participants. The depositary will credit, on its book-entry registration and transfer system, the respective principal amounts of debt securities represented by the global security to the accounts of its participants.

Ownership of beneficial interests in a global security will be shown on and effected through records maintained by the depositary, with respect to participants' interests, or any participant, with respect to interests of persons held by participants on their behalf.

Payments, transfers and exchanges relating to beneficial interests in a global security will be subject to policies and procedures of the depositary. The depositary policies and procedures may change from time to time. Neither any trustee nor we will have any responsibility or liability for the depositary's or any participant's records with respect to beneficial interests in a global security.

Payment and Paying Agents

Unless otherwise indicated in a prospectus supplement, the provisions described in this paragraph will apply to the debt securities. Payment of interest on a debt security on any interest payment date will be made to the person in whose name the debt security is registered at the close of business on the regular record date. Payment on debt securities of a particular series will be payable at the office of a paying agent or paying agents designated by us. However, at our option, we may pay interest by mailing a check to the record holder. The trustee will be designated as our initial paying agent.

We may also name any other paying agents in a prospectus supplement. We may designate additional paying agents, change paying agents or change the office of any paying agent. However, we will be required to maintain a paying agent in each place of payment for the debt securities of a particular series.

All moneys paid by us to a paying agent for payment on any debt security that remain unclaimed for a period ending the earlier of:

- 10 business days prior to the date the money would be turned over to the applicable state; or
- at the end of two years after such payment was due,

will be repaid to us thereafter. The holder may look only to us for such payment.

No Protection in the Event of a Change of Control

Unless otherwise indicated in a prospectus supplement with respect to a particular series of debt securities, the debt securities will not contain any provisions that may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly-leveraged transaction, whether or not such transaction results in a change in control.

Covenants

Unless otherwise indicated in a prospectus supplement with respect to a particular series of debt securities, the debt securities will not contain any financial or restrictive covenants.

Consolidation, Merger and Sale of Assets

Unless we indicate otherwise in a prospectus supplement with respect to a particular series of debt securities, we may not consolidate with or merge into any other person (other than one of our subsidiaries), in a transaction in which we are not the surviving corporation, or convey, transfer or lease our properties and assets substantially as an entirety to, any person (other than to one or more subsidiaries of Otonomy, Inc.), unless:

- the successor entity, if any, is a U.S. corporation, limited liability company, partnership, trust or other business entity;
- the successor entity assumes our obligations on the debt securities and under the indentures;
- immediately after giving effect to the transaction, no default or event of default shall have occurred and be continuing; and
- certain other conditions specified in the applicable indenture are met.

Events of Default

Unless we indicate otherwise in a prospectus supplement, the following will be events of default for any series of debt securities under the indentures:

(1) we fail to pay principal of or any premium or the redemption price on any debt security of that series when due;

(2) we fail to pay any interest on any debt security of that series for 30 days after it becomes due;

(3) we fail to deposit any sinking fund payment when due;

(4) we default or breach any covenant or warranty in the applicable indenture and such failure continues for 90 days after we are given the notice required in the indentures; and

(5) certain events involving our bankruptcy, insolvency or reorganization.

Additional or different events of default applicable to a series of debt securities may be described in a prospectus supplement. An event of default of one series of debt securities is not necessarily an event of default for any other series of debt securities.

The trustee may withhold notice to the holders of any default, except defaults in the payment of principal, premium, if any, interest, any sinking fund installment on, or with respect to any conversion right of, the debt securities of such series. However, the trustee must consider it to be in the interest of the holders of the debt securities of such series to withhold this notice.

Unless we indicate otherwise in a prospectus supplement, if an event of default, other than an event of default described in clause (5) above, shall occur and be continuing with respect to any series of debt securities, either the trustee or the holders of at least 25% in aggregate principal amount of the outstanding securities of that series may declare the principal amount and premium, if any, of the debt securities of that series, or if any debt securities of that series are original issue discount securities, such other amount as may be specified in the applicable prospectus supplement, in each case together with accrued and unpaid interest thereon, if any, to be due and payable immediately.

Unless we indicate otherwise in a prospectus supplement, if an event of default described in clause (5) above shall occur, the principal amount and premium, if any, of all the debt securities of that series, or if any

debt securities of that series are original issue discount securities, such other amount as may be specified in the applicable prospectus supplement, in each case together with accrued and unpaid interest thereon, if any, will automatically become immediately due and payable. Any payment by us on the subordinated debt securities following any such acceleration will be subject to the subordination provisions described below under "Subordinated Debt Securities."

Notwithstanding the foregoing, each indenture will provide that we may, at our option, elect that the sole remedy for an event of default relating to our failure to comply with our obligations described under the section entitled "Reports" below or our failure to comply with the requirements of Section 314(a)(1) of the Trust Indenture Act will for the first 360 days after the occurrence of such an event of default consist exclusively of the right to receive additional interest on the relevant series of debt securities at an annual rate equal to (1) 0.25% of the principal amount of such series of debt securities for the first 180 days after the occurrence of such event of default and (2) 0.50% of the principal amount of such series of debt securities from the 181st day to, and including, the 360th day after the occurrence of such event of default, which we call "additional interest." If we so elect, the additional interest will accrue on all outstanding debt securities from and including the date on which such event of default first occurs until such violation is cured or waived and shall be payable on each relevant interest payment date to holders of record on the regular record date immediately preceding the interest payment date. On the 361st day after such event of default (if such violation is not cured or waived prior to such 361st day), the debt securities will be subject to acceleration as provided above. In the event we do not elect to pay additional interest upon any such event of default in accordance with this paragraph, the debt securities will be subject to acceleration as provided above.

In order to elect to pay the additional interest as the sole remedy during the first 360 days after the occurrence of any event of default relating to the failure to comply with the reporting obligations in accordance with the preceding paragraph, we must notify all holders of debt securities and the trustee and paying agent of such election prior to the close of business on the first business day following the date on which such event of default occurs. Upon our failure to timely give such notice or pay the additional interest, the debt securities will be immediately subject to acceleration as provided above.

After acceleration, the holders of a majority in aggregate principal amount of the outstanding securities of that series may, under certain circumstances, rescind and annul such acceleration if all events of default, other than the non-payment of accelerated principal, or other specified amounts or interest, have been cured or waived.

Other than the duty to act with the required care during an event of default, the trustee will not be obligated to exercise any of its rights or powers at the request of the holders unless the holders shall have offered to the trustee reasonable indemnity. Generally, the holders of a majority in aggregate principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee.

A holder of debt securities of any series will not have any right to institute any proceeding under the indentures, or for the appointment of a receiver or a trustee, or for any other remedy under the indentures, unless:

(1) the holder has previously given to the trustee written notice of a continuing event of default with respect to the debt securities of that series;

(2) the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made a written request and have offered reasonable indemnity to the trustee to institute the proceeding; and

(3) the trustee has failed to institute the proceeding and has not received direction inconsistent with the original request from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series within 60 days after the original request.

Holders may, however, sue to enforce the payment of principal, premium or interest on any debt security on or after the due date or to enforce the right, if any, to convert any debt security (if the debt security is convertible) without following the procedures listed in (1) through (3) above.

We will furnish the trustee an annual statement from our officers as to whether or not we are in default in the performance of the conditions and covenants under the applicable indenture and, if so, specifying all known defaults.

Modification and Waiver

Unless we indicate otherwise in a prospectus supplement, the applicable trustee and we may make modifications and amendments to an indenture with the consent of the holders of a majority in aggregate principal amount of the outstanding securities of each series affected by the modification or amendment.

We may also make modifications and amendments to the indentures for the benefit of holders without their consent, for certain purposes including, but not limited to:

- to evidence the succession of another person to Otonomy, or successive successions, and the assumption by any such successor of the covenants of Otonomy in the indentures in compliance with Article 8 of the indentures;
- adding covenants for the benefit of holders or surrendering any right or power conferred upon Otonomy;
- adding events of default for the benefit of holders;
- making certain changes to facilitate the issuance of the debt securities in bearer form, registrable or not registrable as to the principal, with or without interest coupons, or to permit or facilitate the issuance of debt securities in uncertificated form;
- to add to, change or eliminate any of the provisions of the indentures or series of securities, provided that any such addition, change or elimination (1) shall neither (a) apply to any security of any series created prior to the execution of such supplemental indenture and entitled to the benefit of such provision nor (b) modify the rights of the holder of any such security with respect to such provision or (2) shall become effective only when there is no such security outstanding;
- securing the debt securities, including provisions regarding the circumstances under which collateral may be released and substituted;
- providing for guaranties of, or adding additional obligors on, the debt securities;
- to establish the form or term of debt securities as permitted by Sections 2.1 and 3.1 of the indentures;
- providing for a successor trustee or additional trustees;
- conforming the indentures to the description of the securities set forth in this prospectus or the accompanying prospectus supplement;
- curing any ambiguity, defect or inconsistency or to make any other provisions with respect to matters or questions arising under the indentures;
- supplementing any of the provisions of the indentures to such extent as shall be necessary to permit or facilitate the defeasance and discharge of the debt securities, provided that such action shall not adversely affect the interest of the holders in any material respect;
- make such other provisions in regard to matters or questions arising under the indentures or under any supplemental indentures as our board of directors may deem necessary or desirable, and which does not in each case adversely affect the interests of the holders of the debt securities of a series; and

- comply with requirements of the SEC in order to effect or maintain the qualifications of the indentures under the Trust Indenture Act of 1939, as amended (the "Trust Indenture Act").

However, neither the trustee nor we may make any modification or amendment without the consent of the holder of each outstanding security of that series affected by the modification or amendment if such modification or amendment would:

- change the stated maturity of the principal of, or any installment of principal or interest on, any debt security;
- reduce the principal, premium, if any, or interest on any debt security or any premium payable upon redemption or repurchase, whether at our option or the option of any holder, or reduce the amount of any sinking fund payments;
- reduce the principal of an original issue discount security or any other debt security payable on acceleration of maturity;
- change the place of payment or the currency in which any debt security is payable;
- impair the right to enforce any payment after the stated maturity (or in the case of redemption, on or after the redemption date);
- if subordinated debt securities, modify the subordination provisions in a materially adverse manner to the holders;
- adversely affect the right to convert any debt security if the debt security is a convertible debt security; or
- change the provisions in the indentures that relate to modifying or amending the indentures.

Satisfaction and Discharge; Defeasance

We may be discharged from our obligations on the debt securities, subject to limited exceptions, of any series that have matured or will mature or be redeemed within one year if we deposit enough money with the trustee to pay all the principal, interest and any premium due to the stated maturity date or redemption date of the debt securities.

Each indenture contains a provision that permits us to elect either or both of the following:

- we may elect to be discharged from all of our obligations, subject to limited exceptions, with respect to any series of debt securities then outstanding. If we make this election, the holders of the debt securities of the series will not be entitled to the benefits of the indenture, except for the rights of holders to receive payments on debt securities or the registration of transfer and exchange of debt securities and replacement of lost, stolen or mutilated debt securities.
- we may elect to be released from our obligations under some or all of any financial or restrictive covenants applicable to the series of debt securities to which the election relates and from the consequences of an event of default resulting from a breach of those covenants.

To make either of the above elections, we must irrevocably deposit in trust with the trustee enough money to pay in full the principal, interest and premium on the debt securities. This amount may be made in cash and/or U.S. government obligations or, in the case of debt securities denominated in a currency other than U.S. dollars, cash in the currency in which such series of securities is denominated and/or foreign government obligations. As a condition to either of the above elections, for debt securities denominated in U.S. dollars we must deliver to the trustee an opinion of counsel that the holders of the debt securities will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the action.

With respect to debt securities of any series that are denominated in a currency other than United States dollars, “foreign government obligations” means:

- direct obligations of the government that issued or caused to be issued the currency in which such securities are denominated and for the payment of which obligations its full faith and credit is pledged, or, with respect to debt securities of any series which are denominated in Euros, direct obligations of certain members of the European Union for the payment of which obligations the full faith and credit of such members is pledged, which in each case are not callable or redeemable at the option of the issuer thereof; or
- obligations of a person controlled or supervised by or acting as an agency or instrumentality of a government described in the bullet above the timely payment of which is unconditionally guaranteed as a full faith and credit obligation by such government, which are not callable or redeemable at the option of the issuer thereof.

Notices

Notices to holders will be given by mail to the addresses of the holders in the security register.

Governing Law

The indentures and the debt securities will be governed by, and construed under, the laws of the State of New York.

No Personal Liability of Directors, Officers, Employees and Stockholders

No incorporator, stockholder, employee, agent, officer, director or subsidiary of ours will have any liability for any obligations of ours, or because of the creation of any indebtedness under the debt securities, the indentures or supplemental indentures. The indentures provide that all such liability is expressly waived and released as a condition of, and as a consideration for, the execution of such indentures and the issuance of the debt securities.

Regarding the Trustee

The indentures limit the right of the trustee, should it become our creditor, to obtain payment of claims or secure its claims.

The trustee will be permitted to engage in certain other transactions with us. However, if the trustee acquires any conflicting interest, and there is a default under the debt securities of any series for which it is trustee, the trustee must eliminate the conflict or resign.

Subordinated Debt Securities

The following provisions will be applicable with respect to each series of subordinated debt securities, unless otherwise stated in the prospectus supplement relating to that series of subordinated debt securities.

The indebtedness evidenced by the subordinated debt securities of any series is subordinated, to the extent provided in the subordinated indenture and the applicable prospectus supplement, to the prior payment in full, in cash or other payment satisfactory to the holders of senior debt, of all senior debt, including any senior debt securities.

Upon any distribution of our assets upon any dissolution, winding up, liquidation or reorganization, whether voluntary or involuntary, marshalling of assets, assignment for the benefit of creditors, or in bankruptcy,

insolvency, receivership or other similar proceedings, payments on the subordinated debt securities will be subordinated in right of payment to the prior payment in full in cash or other payment satisfactory to holders of senior debt of all senior debt.

In the event of any acceleration of the subordinated debt securities of any series because of an event of default with respect to the subordinated debt securities of that series, holders of any senior debt would be entitled to payment in full in cash or other payment satisfactory to holders of senior debt of all senior debt before the holders of subordinated debt securities are entitled to receive any payment or distribution.

In addition, the subordinated debt securities will be structurally subordinated to all indebtedness and other liabilities of our subsidiaries, including trade payables and lease obligations. This occurs because our right to receive any assets of our subsidiaries upon their liquidation or reorganization, and your right to participate in those assets, will be effectively subordinated to the claims of that subsidiary's creditors, including trade creditors, except to the extent that we are recognized as a creditor of such subsidiary. If we are recognized as a creditor of that subsidiary, our claims would still be subordinate to any security interest in the assets of the subsidiary and any indebtedness of the subsidiary senior to us.

We are required to promptly notify holders of senior debt or their representatives under the subordinated indenture if payment of the subordinated debt securities is accelerated because of an event of default.

Under the subordinated indenture, we may not make payment on the subordinated debt securities if:

- a default in our obligations to pay principal, premium, if any, interest or other amounts on our senior debt occurs and the default continues beyond any applicable grace period, which we refer to as a payment default; or
- any other default occurs and is continuing with respect to designated senior debt that permits holders of designated senior debt to accelerate its maturity, which we refer to as a non-payment default, and the trustee receives a payment blockage notice from us or some other person permitted to give the notice under the subordinated indenture.

We will resume payments on the subordinated debt securities:

- in case of a payment default, when the default is cured or waived or ceases to exist, and
- in case of a non-payment default, the earlier of when the default is cured or waived or ceases to exist or 179 days after the receipt of the payment blockage notice.

No new payment blockage period may commence on the basis of a non-payment default unless 365 days have elapsed from the effectiveness of the immediately prior payment blockage notice. No non-payment default that existed or was continuing on the date of delivery of any payment blockage notice to the trustee shall be the basis for a subsequent payment blockage notice.

As a result of these subordination provisions, in the event of our bankruptcy, dissolution or reorganization, holders of senior debt may receive more, ratably, and holders of the subordinated debt securities may receive less, ratably, than our other creditors. The subordination provisions will not prevent the occurrence of any event of default under the subordinated indenture.

The subordination provisions will not apply to payments from money or government obligations held in trust by the trustee for the payment of principal, interest and premium, if any, on subordinated debt securities pursuant to the provisions described under the section entitled "Satisfaction and Discharge; Defeasance," if the subordination provisions were not violated at the time the money or government obligations were deposited into trust.

If the trustee or any holder receives any payment that should not have been made to them in contravention of subordination provisions before all senior debt is paid in full in cash or other payment satisfactory to holders of senior debt, then such payment will be held in trust for the holders of senior debt.

Senior debt securities will constitute senior debt under the subordinated indenture.

Additional or different subordination provisions may be described in a prospectus supplement relating to a particular series of debt securities.

Definitions

"Designated senior debt" means our obligations under any particular senior debt in which the instrument creating or evidencing the same or the assumption or guarantee thereof, or related agreements or documents to which we are a party, expressly provides that such indebtedness shall be designated senior debt for purposes of the subordinated indenture. The instrument, agreement or other document evidencing any designated senior debt may place limitations and conditions on the right of such senior debt to exercise the rights of designated senior debt.

"Indebtedness" means the following, whether absolute or contingent, secured or unsecured, due or to become due, outstanding on the date of the applicable indenture for such series of securities or thereafter created, incurred or assumed:

- our indebtedness evidenced by a credit or loan agreement, note, bond, debenture or other written obligation;
- all of our obligations for money borrowed;
- all of our obligations evidenced by a note or similar instrument given in connection with the acquisition of any businesses, properties or assets of any kind,
- our obligations:
  - as lessee under leases required to be capitalized on the balance sheet of the lessee under generally accepted accounting principles, or
  - as lessee under leases for facilities, capital equipment or related assets, whether or not capitalized, entered into or leased for financing purposes;
- all of our obligations under interest rate and currency swaps, caps, floors, collars, hedge agreements, forward contracts or similar agreements or arrangements;
- all of our obligations with respect to letters of credit, bankers' acceptances and similar facilities, including reimbursement obligations with respect to the foregoing;
- all of our obligations issued or assumed as the deferred purchase price of property or services, but excluding trade accounts payable and accrued liabilities arising in the ordinary course of business;
- all obligations of the type referred to in the above clauses of another person, the payment of which, in either case, we have assumed or guaranteed, for which we are responsible or liable, directly or indirectly, jointly or severally, as obligor, guarantor or otherwise, or which are secured by a lien on our property; and
- renewals, extensions, modifications, replacements, restatements and refundings of, or any indebtedness or obligation issued in exchange for, any such indebtedness or obligation described in the above clauses of this definition.

"Senior debt" means the principal of, premium, if any, and interest, including all interest accruing subsequent to the commencement of any bankruptcy or similar proceeding, whether or not a claim for post-

petition interest is allowable as a claim in any such proceeding, and rent payable on or in connection with, and all fees and other amounts payable in connection with, our indebtedness. However, senior debt shall not include:

- any debt or obligation if its terms or the terms of the instrument under which or pursuant to which it is issued expressly provide that it shall not be senior in right of payment to the subordinated debt securities or expressly provide that such indebtedness is on the same basis or "junior" to the subordinated debt securities; or
- debt to any of our subsidiaries, a majority of the voting stock of which is owned, directly or indirectly, by us.

"Subsidiary" means a corporation more than 50% of the outstanding voting stock of which is owned, directly or indirectly, by us or by one or more of our other subsidiaries or by a combination of us and our other subsidiaries. For purposes of this definition, "voting stock" means stock or other similar interests which ordinarily has or have voting power for the election of directors, or persons performing similar functions, whether at all times or only so long as no senior class of stock or other interests has or have such voting power by reason of any contingency.

DESCRIPTION OF SUBSCRIPTION RIGHTS

We may issue subscription rights to purchase our common stock, preferred stock or debt securities. These subscription rights may be offered independently or together with any other security offered hereby and may or may not be transferable by the stockholder receiving the subscription rights in such offering. In connection with any offering of subscription rights, we may enter into a standby arrangement with one or more underwriters or other purchasers pursuant to which the underwriters or other purchasers may be required to purchase any securities remaining unsubscribed for after such offering.

The prospectus supplement relating to any subscription rights we offer, if any, will, to the extent applicable, include specific terms relating to the offering, including some or all of the following:

- the price, if any, for the subscription rights;
- the exercise price payable for our common stock, preferred stock or debt securities upon the exercise of the subscription rights;
- the number of subscription rights to be issued to each stockholder;
- the number and terms of our common stock, preferred stock or debt securities which may be purchased per each subscription right;
- the extent to which the subscription rights are transferable;
- any other terms of the subscription rights, including the terms, procedures and limitations relating to the exchange and exercise of the subscription rights;
- the date on which the right to exercise the subscription rights shall commence, and the date on which the subscription rights shall expire;
- the extent to which the subscription rights may include an over-subscription privilege with respect to unsubscribed securities or an over-allotment privilege to the extent the securities are fully subscribed; and
- if applicable, the material terms of any standby underwriting or purchase arrangement which may be entered into by Otonomy in connection with the offering of subscription rights.

The description in the applicable prospectus supplement of any subscription rights we offer will not necessarily be complete and will be qualified in its entirety by reference to the applicable subscription rights certificate, which will be filed with the SEC if we offer subscription rights. We urge you to read the applicable subscription rights certificate and any applicable prospectus supplement in their entirety.

DESCRIPTION OF UNITS

We may issue units comprising one or more of the other classes of securities described in this prospectus in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The units may be issued under unit agreements to be entered into between us and a unit agent, as detailed in the prospectus supplement relating to the units being offered. The prospectus supplement will describe:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances the securities comprising the units may be held or transferred separately;
- a description of the terms of any unit agreement governing the units;
- a description of the provisions for the payment, settlement, transfer or exchange of the units;
- a discussion of material federal income tax considerations, if applicable; and
- whether the units if issued as a separate security will be issued in fully registered or global form.

The descriptions of the units in this prospectus and in any prospectus supplement are summaries of the material provisions of the applicable unit agreements. These descriptions do not restate those unit agreements in their entirety and may not contain all the information that you may find useful. We urge you to read the applicable unit agreements because they, and not the summaries, define your rights as holders of the units. For more information, please review the forms of the relevant unit agreements, which will be filed with the SEC promptly after the offering of units and will be available as described in the section titled “Where You Can Find More Information.”

PLAN OF DISTRIBUTION

We may sell the securities offered through this prospectus (1) to or through underwriters or dealers, (2) directly to purchasers, including our affiliates, (3) through agents, or (4) through a combination of any of these methods. The securities may be distributed at a fixed price or prices, which may be changed, market prices prevailing at the time of sale, prices related to the prevailing market prices, or negotiated prices. The prospectus supplement will include the following information:

- the terms of the offering;
- the names of any underwriters or agents;
- the name or names of any managing underwriter or underwriters;
- the purchase price of the securities;
- the net proceeds from the sale of the securities;
- any delayed delivery arrangements;
- any underwriting discounts, commissions or agency fees, and other items constituting underwriters' or agents' compensation;
- any initial price to the public;
- any discounts or concessions allowed or reallowed or paid to dealers; and
- any commissions paid to agents.

We may engage in at-the-market offerings into an existing trading market in accordance with Rule 415(a)(4) in the manner described below under "—At-the-Market Offerings."

We may issue to the holders of our common stock, on a pro rata basis for no consideration, subscription rights to purchase shares of our common stock or preferred stock. These subscription rights may or may not be transferable by stockholders. The applicable prospectus supplement will describe the specific terms of any offering of our common or preferred stock through the issuance of subscription rights, including the terms of the subscription rights offering, the terms, procedures and limitations relating to the exchange and exercise of the subscription rights and, if applicable, the material terms of any standby underwriting or purchase arrangement entered into by us in connection with the offering of common or preferred stock through the issuance of subscription rights.

Sale through Underwriters or Dealers

If underwriters are used in the sale, the underwriters will acquire the securities for their own account, including through underwriting, purchase, security lending or repurchase agreements with us. The underwriters may resell the securities from time to time in one or more transactions, including negotiated transactions. Underwriters may sell the securities in order to facilitate transactions in any of our other securities (described in this prospectus or otherwise), including other public or private transactions and short sales. Underwriters may offer securities to the public either through underwriting syndicates represented by one or more managing underwriters or directly by one or more firms acting as underwriters. Unless otherwise indicated in the prospectus supplement, the obligations of the underwriters to purchase the securities will be subject to certain conditions, and the underwriters will be obligated to purchase all the offered securities if they purchase any of them (other than any securities purchased upon exercise of any option to purchase additional securities). In connection with any offering of common stock pursuant to this prospectus, underwriters may have an option to purchase additional shares of common stock from us. We will provide information regarding any such option to purchase additional shares of common stock from us in the applicable prospectus supplement. The underwriters may change from time to time any initial price to the public and any discounts or concessions allowed or

reallowed or paid to dealers. The prospectus supplement will include the names of the principal underwriters the respective amount of securities underwritten, the nature of the obligation of the underwriters to take the securities and the nature of any material relationship between an underwriter and us.

Some or all of the securities that we offer through this prospectus may be new issues of securities with no established trading market. Any underwriters to whom we sell securities for public offering and sale may make a market in those securities, but they will not be obligated to do so and they may discontinue any market making at any time without notice. Accordingly, we cannot assure you of the liquidity of, or continued trading markets for, any securities offered pursuant to this prospectus.

If dealers are used in the sale of securities offered through this prospectus, we will sell the securities to them as principals. They may then resell those securities to the public at varying prices determined by the dealers at the time of resale. The prospectus supplement will include the names of the dealers and the terms of the transaction.

Direct Sales and Sales through Agents

We may sell the securities offered through this prospectus directly. In this case, no underwriters or agents would be involved. Such securities may also be sold through agents designated from time to time. The prospectus supplement will name any agent involved in the offer or sale of the offered securities and will describe any commissions payable to the agent by us. Unless otherwise indicated in the prospectus supplement, any agent will agree to use its reasonable best efforts to solicit purchases for the period of its appointment.

We may sell the securities directly to institutional investors or others who may be deemed to be underwriters within the meaning of the Securities Act with respect to any sale of those securities. The terms of any such sales will be described in the prospectus supplement.

Delayed Delivery Contracts

If the prospectus supplement indicates, we may authorize agents, underwriters or dealers to solicit offers from certain types of institutions to purchase securities at the public offering price under delayed delivery contracts. These contracts would provide for payment and delivery on a specified date in the future. The contracts would be subject only to those conditions described in the prospectus supplement. The applicable prospectus supplement will describe the commission payable for solicitation of those contracts.

At-the-Market Offerings

To the extent that we make sales through one or more underwriters or agents in at-the-market offerings, we will do so pursuant to the terms of a sales agency financing agreement or other at-the-market offering arrangement between us, on one hand, and the underwriters or agents, on the other. If we engage in at-the-market sales pursuant to any such agreement, we will issue and sell our securities through one or more underwriters or agents, which may act on an agency basis or a principal basis. During the term of any such agreement, we may sell securities on a daily basis in exchange transactions or otherwise as we agree with the underwriters or agents. Any such agreement will provide that any securities sold will be sold at prices related to the then prevailing market prices for our securities. Therefore, exact figures regarding proceeds that will be raised or commissions to be paid cannot be determined as of the date of this prospectus. Pursuant to the terms of the agreement, we may agree to sell, and the relevant underwriters or agents may agree to solicit offers to purchase, blocks of our common stock or other securities. The terms of any such agreement will be set forth in more detail in the applicable prospectus or prospectus supplement.

Market Making, Stabilization and Other Transactions

Unless the applicable prospectus supplement states otherwise, each series of offered securities will be a new issue and will have no established trading market. We may elect to list any series of offered securities on an

exchange. Any underwriters that we use in the sale of offered securities may make a market in such securities, but may discontinue such market making at any time without notice. Therefore, we cannot assure you that the securities will have a liquid trading market.

Any underwriter may also over-allot or engage in stabilizing transactions, syndicate covering transactions and penalty bids in accordance with Rule 104 of Regulation M under the Exchange Act. Over-allotment or short sales involve sales by persons participating in the offering of more securities than were sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option, if any. Stabilizing transactions involve bids to purchase the underlying security in the open market for the purpose of pegging, fixing or maintaining the price of the securities. Syndicate covering transactions involve purchases of the securities in the open market after the distribution has been completed in order to cover syndicate short positions.

Penalty bids permit the underwriters to reclaim a selling concession from a syndicate member when the securities originally sold by the syndicate member are purchased in a syndicate covering transaction to cover syndicate short positions. These transactions may cause the price of the securities to be higher than it would be in the absence of the transactions. The underwriters may, if they commence these transactions, discontinue them at any time.

Derivative Transactions and Hedging

We, the underwriters or other agents may engage in derivative transactions involving the securities. These derivatives may consist of short sale transactions and other hedging activities. The underwriters or agents may acquire a long or short position in the securities, hold or resell securities acquired and purchase options or futures on the securities and other derivative instruments with returns linked to or related to changes in the price of the securities. In order to facilitate these derivative transactions, we may enter into security lending or repurchase agreements with the underwriters or agents. The underwriters or agents may effect the derivative transactions through sales of the securities to the public, including short sales, or by lending the securities in order to facilitate short sale transactions by others. The underwriters or agents may also use the securities purchased or borrowed from us or others (or, in the case of derivatives, securities received from us in settlement of those derivatives) to directly or indirectly settle sales of the securities or close out any related open borrowings of the securities.

Electronic Auctions

We may also make sales through the Internet or through other electronic means. Since we may from time to time elect to offer securities directly to the public, with or without the involvement of agents, underwriters or dealers, utilizing the Internet or other forms of electronic bidding or ordering systems for the pricing and allocation of such securities, you should pay particular attention to the description of that system we will provide in a prospectus supplement.

Such electronic system may allow bidders to directly participate, through electronic access to an auction site, by submitting conditional offers to buy that are subject to acceptance by us, and which may directly affect the price or other terms and conditions at which such securities are sold. These bidding or ordering systems may present to each bidder, on a so-called “real-time” basis, relevant information to assist in making a bid, such as the clearing spread at which the offering would be sold, based on the bids submitted, and whether a bidder’s individual bids would be accepted, prorated or rejected. For example, in the case of a debt security, the clearing spread could be indicated as a number of “basis points” above an index treasury note. Of course, many pricing methods can and may also be used.

Upon completion of such an electronic auction process, securities will be allocated based on prices bid, terms of bid or other factors. The final offering price at which securities would be sold and the allocation of securities among bidders would be based in whole or in part on the results of the Internet or other electronic bidding process or auction.

General Information

Agents, underwriters, and dealers may be entitled, under agreements entered into with us, to indemnification by us against certain liabilities, including liabilities under the Securities Act. Our agents, underwriters, and dealers, or their affiliates, may engage in transactions with, or perform services for us in the ordinary course of business.

LEGAL MATTERS

The validity of the securities offered by this prospectus will be passed upon by Wilson Sonsini Goodrich & Rosati, P.C., Palo Alto, California. Certain members of, and investment partnerships comprised of members of, and persons associated with, Wilson Sonsini Goodrich & Rosati, Professional Corporation, own an aggregate of 15,627 shares of our common stock. Additional legal matters may be passed on for us, or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and other reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at http://www.sec.gov. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the Public Reference Room. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K, including any amendments to those reports, and other information that we file with or furnish to the SEC pursuant to Section 13(a) or 15(d) of the Exchange Act can also be accessed free of charge through the Internet. These filings will be available as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

We have filed with the SEC a registration statement under the Securities Act of 1933 relating to the offering of these securities. The registration statement, including the attached exhibits, contains additional relevant information about us and the securities. This prospectus does not contain all of the information set forth in the registration statement. You can obtain a copy of the registration statement, at prescribed rates, from the SEC at the address listed above. The registration statement and the documents referred to below under "Information Incorporated by Reference" are also available on our Internet website, www.otonomy.com. We have not incorporated by reference into this prospectus the information on our website, and you should not consider it to be a part of this prospectus.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus certain information we file with it, which means that we can disclose important information by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus, and information that we file later with the SEC will automatically update and supersede information contained in this prospectus and any accompanying prospectus supplement. We incorporate by reference the documents listed below that we have previously filed with the SEC (excluding any portions of any Form 8-K that are not deemed "filed" pursuant to the General Instructions of Form 8-K):

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, filed with the SEC on March 8, 2018;
- the information specifically incorporated by reference into the Annual Report from our definitive proxy statement on Schedule 14A, filed with the SEC on April 27, 2018;
- our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2018 (filed with the SEC on May 9, 2018) and June 30, 2018 (filed with the SEC on August 8, 2018);
- our Current Report on Form 8-K filed with the SEC on June 21, 2018; and
- the description of our common stock contained in our Registration Statement on Form 8-A as filed with the SEC on August 5, 2014 pursuant to Section 12(b) of the Exchange Act.

We also incorporate by reference into this prospectus additional documents that we may file with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the completion or termination of the offering, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information deemed furnished and not filed with the SEC. Any statements contained in a previously filed document incorporated by reference into this prospectus is deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus, or in a subsequently filed document also incorporated by reference herein, modifies or supersedes that statement.

This prospectus may contain information that updates, modifies or is contrary to information in one or more of the documents incorporated by reference in this prospectus. You should rely only on the information incorporated by reference or provided in this prospectus. We have not authorized anyone else to provide you with different information. You should not assume that the information in this prospectus is accurate as of any date other than the date of this prospectus or the date of the documents incorporated by reference in this prospectus.

We will provide to each person, including any beneficial owner, to whom this prospectus is delivered, upon written or oral request, at no cost to the requester, a copy of any and all of the information that is incorporated by reference in this prospectus.

Requests for such documents should be directed to:

Otonomy, Inc.
4796 Executive Drive
San Diego, California 92121
Attention: Secretary

You may also access the documents incorporated by reference in this prospectus through our website at www.otonomy.com. Except for the specific incorporated documents listed above, no information available on or through our website shall be deemed to be incorporated in this prospectus or the registration statement of which it forms a part.

14,500,000 Shares of Common Stock

Pre-Funded Warrants to Purchase 4,000,000 Shares of Common Stock

PROSPECTUS SUPPLEMENT

Joint Book-Running Managers

Cowen **Piper Sandler** **Cantor**

Lead Manager

H.C. Wainwright & Co.

July 9, 2020