OTONOMY®

Targeted Medicines for the Ear

2021 | ANNUAL REPORT

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2021

OR

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

FOR THE TRANSITION PERIOD FROM _____ TO

Commission file number 001-36591

Otonomy, Inc.

(Exact name of registrant as specified in its charter)

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

4796 Executive Drive
San Diego, California 92121
(Address of principal executive offices and Zip Code)

(619) 323-2200
(Registrant's telephone number, including area code)

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

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

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

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

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

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

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

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

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
Emerging growth company	☐		

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☒

The aggregate market value of the common stock held by non-affiliates of the registrant as of June 30, 2021 (the last business day of the registrant's most recently completed second fiscal quarter) was approximately $96.6 million based on the closing price of the registrant's common stock, as reported by the NASDAQ Global Select Market on June 30, 2021 of $2.23 per share. Shares of the registrant's common stock held by executive officers, directors and their affiliates have been excluded from this calculation. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of February 22, 2022, the number of outstanding shares of the registrant's common stock, par value $0.001 per share, was 56,732,474.

DOCUMENTS INCORPORATED BY REFERENCE

As noted herein, the information called for by Part III is incorporated by reference to specified portions of the registrant's definitive proxy statement to be filed in conjunction with the registrant's 2022 Annual Meeting of Stockholders, which is expected to be filed not later than 120 days after the registrant's fiscal year ended December 31, 2021.

OTONOMY, INC.
ANNUAL REPORT ON FORM 10-K
FOR THE YEAR ENDED DECEMBER 31, 2021
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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, which statements involve substantial risks and uncertainties. Forward-looking statements generally relate to future events or our future financial or operating performance. In some cases, you can identify forward-looking statements because they contain words such as "anticipate," "believe," "could," "estimate," "expects," "intend," "may," "plan," "potential," "predict," "project," "should," "will," "would" the negative of those terms, and similar expressions that convey uncertainty of future events or outcomes. Forward-looking statements contained in this Annual Report on Form 10-K include, but are not limited to, statements concerning the following:

- 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 in tinnitus patients, including availability of top-line results from the ongoing Phase 2 clinical trial and clinical safety evaluation of higher and bilateral dosing of OTO-313;
- our expectations regarding the clinical development of OTO-413 in hearing loss patients, including availability of top-line results from the ongoing Phase 2a cohort and ongoing clinical evaluation of at least one higher dose of OTO-413;
- our expectations regarding the future development of OTO-825 for congenital hearing loss and our collaboration with Applied Genetic Technologies Corporation (AGTC);
- 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 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 obtain 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;
- our expectations regarding the benefits of the loans provided by Oxford Finance LLC;
- our financial performance;
- our expectations and statements regarding the benefits, pricing, market size, opportunity and growth potential for OTO-313, OTO-413, OTO-825 and our other product candidates, if approved for commercial use;
- our expectations and statements regarding the adoption and use of OTO-313, OTO-413 and OTO-825, if approved;
- our expectations regarding potential coverage and reimbursement relating to OTO-313, OTO-413 and OTO-825, if approved, or any other approved product candidates;
- accounting principles, policies and estimates; and
- developments and projections relating to our competitors and our industry.

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; the advancement of our product candidates, such as OTO-313, OTO-413 and OTO-825 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 our product candidates; our ability to protect our intellectual property related to our product candidates in the United States and throughout the world; expectations regarding potential market size, opportunity and growth; our ability to manage operating expenses; implementation of our business model and strategic plans for our business, 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 loans 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 Annual Report on Form 10-K and are subject to risks and uncertainties.

We discuss many of these risks in greater detail in the section titled “Risk Factors” included in Part I, Item 1A and elsewhere in this report. 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 Annual Report on Form 10-K 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.

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

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

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

PART I

Item 1. BUSINESS

Overview

Otonomy is a biopharmaceutical company dedicated to the development of innovative therapeutics for neurotology. We pioneered the application of drug delivery technology to the ear and are utilizing that expertise and proprietary position to develop products that achieve sustained drug exposure from a single local administration. Our primary focus is currently on the advancement of three programs in our broad pipeline: OTO-313 in Phase 2 for tinnitus; OTO-413 in Phase 2a for hearing loss; and OTO-825, a gene therapy for congenital hearing loss, in investigational new drug (IND)-enabling activities. Additionally, we are conducting preclinical development of OTO-510 for otoprotection and OTO-6XX for severe hearing loss. We estimate, based on an external market report commissioned by us, that approximately 28 million people in the United States suffer from moderate to severe tinnitus or hearing loss.

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. In July 2020, we announced positive top-line results from a Phase 1/2 clinical trial of OTO-313 in patients with persistent tinnitus of at least moderate severity. We have completed enrollment in a Phase 2 clinical trial for OTO-313, with top-line results expected in mid-2022. We are also initiating clinical safety evaluations for higher and bilateral dosing of OTO-313, with top-line results expected in the second half of 2022. If positive, we expect these clinical data to support an End-of-Phase 2 meeting with the United States Food and Drug Administration (FDA) and inform the design of the OTO-313 Phase 3 clinical program planned to start in the first half of 2023.

OTO-413 is a sustained-exposure formulation of brain-derived neurotrophic factor (BDNF) in development for the treatment of hearing loss. In December 2020, we announced positive top-line results from a Phase 1/2 clinical trial of OTO-413 across multiple speech-in-noise hearing tests. We have completed enrollment in a Phase 2a cohort for OTO-413, with top-line results expected early in the second quarter of 2022. Additionally, we have initiated enrollment to evaluate higher dosing of OTO-413, with top-line results expected in the second half of 2022. Based on results from the Phase 2a cohort and higher-dose evaluation, we plan to initiate a full dose-ranging Phase 2 efficacy trial by the end of 2022.

OTO-825 is a gene therapy targeting mutations in the gap junction beta-2 (GJB2) gene, which is the most common cause of congenital hearing loss. Preclinical proof-of-concept results for OTO-825 demonstrate that a single administration of OTO-825 rescues hearing loss and cochlear damage in two preclinical models representing a range of hearing loss severity caused by GJB2 deficiency. We have completed a Pre-IND meeting with the FDA that provided guidance regarding nonclinical study design, manufacturing requirements and clinical trial considerations. Based on this feedback, we have initiated IND-enabling activities that we expect to support an IND filing in the first half of 2023.

OTO-510 is a product candidate in preclinical development for the prevention of cisplatin-induced hearing loss (CIHL), which routinely occurs in patients undergoing treatment with this chemotherapeutic agent. OTO-510 has demonstrated improved otoprotection in preclinical studies compared to other drug candidates in clinical development, and is being formulated to provide sustained exposure from a single intratympanic injection. The goal of the OTO-510 program is to preserve hearing without protecting the tumor.

Our OTO-6XX program is evaluating the treatment of severe hearing loss by repairing or regenerating auditory hair cells. In July 2020, we entered into an exclusive license agreement with Kyorin Pharmaceutical Co., Ltd. (Kyorin) that provides us with exclusive worldwide rights to develop, manufacture and commercialize a novel compound from Kyorin for this program.

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 sites' ability to enroll patients, among other activities. 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 following directives from the State of California and the applicable local governments, and guidance from the U.S. Centers for Disease Control and Prevention (CDC). Various safety protocols have been implemented and we are currently allowing employees who can remotely perform their essential functions to work from home as this was determined to be in the best interest of our employees and the communities in which we operate.

Our Product Pipeline

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

Program (Compound)	*Target Population*	*Stage of Development*
OTO-313 (gacyclidine)	Tinnitus	Phase 2
OTO-413 (BDNF)	Hearing Loss	Phase 2a
OTO-825 (GJB2 gene therapy)	Congenital Hearing Loss	IND-enabling
OTO-510 (otoprotectant)	Cisplatin-Induced Hearing Loss	Preclinical development
OTO-6XX (hair cell repair and regeneration)	Severe Hearing Loss	Preclinical development

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

OTO-313 is a sustained-exposure formulation of the NMDA receptor antagonist gacyclidine in development for the treatment of tinnitus. Tinnitus is often described as a ringing in the ear but can also sound like roaring, clicking, hissing or buzzing. There are approximately 8 million people in the United States with moderate or severe tinnitus who may have trouble hearing, working and sleeping. At this time, there is no cure for tinnitus and there are no FDA-approved drugs for the treatment of this debilitating condition. Historic and emerging clinical data provide support for the use of NMDA receptor antagonists, including gacyclidine, for the treatment of tinnitus. Mechanistically, agents from this therapeutic class may act to reduce dysfunctional activity resulting from injury to the hearing organ, or cochlea, and be perceived by the patient as tinnitus.

In July 2020, we announced positive top-line results from a Phase 1/2 clinical trial of OTO-313 in patients with persistent, unilateral tinnitus of at least moderate severity. This trial demonstrated a positive clinical response for a single intratympanic injection of OTO-313 (0.32 mg) using the Tinnitus Functional Index (TFI) that was correlated with tinnitus loudness, tinnitus annoyance and patient global impression of change measures. Based on these results, we initiated a Phase 2 trial that recently completed the enrollment of 153 patients with persistent, unilateral tinnitus of at least moderate severity (target enrollment was 140 patients). Patients were randomized 1:1 to a single intratympanic injection of OTO-313 (0.32 mg) or placebo and are being followed for four months. The primary endpoint is the same as reported for the successful Phase 1/2 trial: a responder analysis based on the proportion of patients who report a clinically meaningful improvement in the TFI from baseline to Months 1 and 2 following treatment. To assess durability of the OTO-313 treatment effect, the follow-up period has been extended out to four months. Top-line results for all timepoints are expected to be available in mid-2022. Additionally, we are initiating a one-month safety study for bilateral and higher (0.64 mg) dosing of OTO-313, with results expected in the second half of 2022. Together, if positive, these clinical data are expected to support an End-of-Phase 2 meeting with the FDA and inform the design of the Phase 3 clinical program for OTO-313 planned to start in the first half of 2023.

Development Programs for the Treatment of Sensorineural Hearing Loss

Hearing loss is a large and growing unmet need with estimates by the World Health Organization that more than 360 million people worldwide have disabling levels of loss. This leads to social isolation, lower quality of life and higher rates of dementia and depression. Common causes include aging, noise, exposure to ototoxic drugs and

genetics, with increased noise exposure from use of recreational music devices accelerating the onset of hearing loss. The pathologies of hearing loss typically involve damage to hair cells and/or auditory nerve fibers in the inner ear. As briefly described below, we are advancing four distinct hearing loss programs targeting different pathologies: repair of cochlear synaptopathy for treatment of speech-in-noise hearing loss (OTO-413), a gene therapy for the most common cause of congenital hearing loss (OTO-825), protection of hair cells from ototoxic drugs including cisplatin chemotherapy (OTO-510), and hair cell repair and regeneration for treatment of severe hearing loss (OTO-6XX).

OTO-413: Sustained-Exposure Neurotrophic Growth Factor for Speech-in-Noise Hearing Loss

Recent research has shown that the loss of synaptic connections between inner ear hair cells and auditory nerve fibers contributes to hearing impairment and may occur earlier than the loss of cochlear hair cells. This cochlear synaptopathy is proposed as an underlying pathology in age-related and noise-induced hearing loss and is believed to contribute to difficulty hearing speech in the presence of background noise, which is the most common complaint of patients seeking treatment for hearing loss. Overall, there are more than 60 million people in the U.S. with hearing loss including approximately 20 million with moderate to severe impairment. This can lead to social isolation, depression and early cognitive decline. Hearing aids provide limited benefit for speech-in-noise hearing problems and there is no FDA-approved drug treatment for this condition.

OTO-413 is a proprietary, sustained-exposure formulation of BDNF, which is a naturally occurring protein involved in neuron growth and repair. Nonclinical studies have demonstrated that local administration of BDNF repairs the connections between inner hair cells and auditory nerve fibers in the cochlea that are damaged due to noise trauma or exposure to ototoxic chemicals. Furthermore, we have demonstrated in preclinical studies that repair of synaptic connections is associated with a restoration of hearing function.

In December 2020, we announced positive top-line results from a Phase 1/2 clinical trial of OTO-413 in subjects with hearing loss. The randomized, double-blind, placebo-controlled, ascending dose trial demonstrated that a single intratympanic injection of OTO-413 was well-tolerated across all dose cohorts. Furthermore, there was demonstration of therapeutic activity of OTO-413 versus placebo across multiple clinically-validated speech-in-noise hearing tests at consecutive time points (Days 57 and 85). In the fourth quarter of 2021, we completed enrollment in a Phase 2a cohort for the highest OTO-413 dose (0.3 mg) evaluated in the initial Phase 1/2 trial cohorts. A total of 33 patients with hearing loss were randomized 2:1 to receive a single intratympanic injection of OTO-413 or placebo. Patients are being followed for three months and assessed using three clinically-validated speech-in-noise hearing tests, with top-line results expected early in the second quarter of 2022. In addition, we are enrolling patients to evaluate at least one higher dose of OTO-413 (starting with 0.75 mg). Each dose cohort will enroll approximately 12 hearing loss patients randomized 2:1 to OTO-413 or placebo, with top-line results expected in the second half of 2022. Based on results from the Phase 2a and higher-dose evaluation, Otonomy expects to initiate a full dose-ranging Phase 2 efficacy trial for OTO-413 by the end of 2022.

OTO-825: GJB2 Gene Therapy Program for Congenital Hearing Loss

Congenital hearing loss is a significant unmet medical need with about 1 out of 500 children born with or developing hearing loss early in life. Genetic mutations are the most common cause of congenital hearing loss and a defect in the GJB2 gene is the most common of these mutations, accounting for approximately 30% of cases. Patients with GJB2 mutation can have severe-to-profound deafness in both ears that is identified in screening tests routinely performed in newborns.

OTO-825 is an adeno-associated virus (AAV)-based gene therapy to restore hearing in patients with a mutation in the GJB2 gene. Preclinical proof-of-concept results, which have been presented at multiple scientific meetings, demonstrate that a single administration of OTO-825 rescues hearing loss and cochlear damage in two preclinical models representing a range of hearing loss severity caused by GJB2 deficiency. We have completed a Pre-IND meeting with the FDA that provided guidance regarding nonclinical study design, manufacturing requirements and clinical trial considerations. Based on this feedback, we are conducting IND-enabling activities that we expect to support an IND filing in the first half of 2023.

In October 2019, we announced a collaboration with AGTC to co-develop and co-commercialize an AAV-based gene therapy for GJB2 deficiency that led to the identification and development of OTO-825. Under the collaboration agreement, Otonomy and AGTC equally shared the program costs and any revenue or other proceeds related to the program through December 31, 2021. Effective January 1, 2022, the collaboration agreement was amended to increase Otonomy's responsibility for the overall development and commercialization of the program, which resulted in: (i) an increase in our share of future product development costs and (ii) our obligation to make potential future payments including royalties on any product sales in lieu of equal sharing of any profits or proceeds related to the program.

OTO-510: Otoprotectant for Cisplatin-Induced Hearing Loss

Cisplatin is a platinum-based chemotherapeutic agent used to treat various tumor types with first-line usage common for testicular, head and neck, and pediatric cancers. According to market estimates, more than 100,000 patients are treated each year with cisplatin in the United States including approximately 5,000 children. While use of cisplatin has contributed to improved patient survival, ototoxicity and associated permanent hearing loss is well documented in the clinical literature. In particular, hearing loss has been reported in up to 90% of children and young adults treated with cisplatin. This adversely affects speech and language development and has been associated with academic and social difficulties which can have a significant impact on patients and their families. At this time, there is no FDA-approved drug treatment to protect against cisplatin-induced hearing loss (CIHL).

OTO-510 is a product candidate in preclinical development for the prevention of CIHL. OTO-510 has demonstrated improved otoprotection in preclinical studies compared to other drug candidates in clinical development, and is being formulated to provide sustained exposure from a single intratympanic injection. The goal of the OTO-510 program is to preserve hearing without protecting the tumor.

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

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

Considerable interest and attention have been focused by otology researchers over the past several decades for ways to regenerate auditory hair cells as an approach to treating severe hearing loss. More recently, researchers have demonstrated the potential to improve hearing through repair of damaged hair cells rather than regeneration, which may be a more technically feasible therapeutic approach. Our OTO-6XX program is evaluating the treatment of severe hearing loss by repairing or regenerating auditory hair cells. In July 2020, we entered into an exclusive license agreement with Kyorin that provides us with exclusive worldwide rights to develop, manufacture and commercialize a novel compound from Kyorin for this program.

Our Proprietary Otic Drug Delivery Technologies

To overcome many of the limitations of delivering drugs to the ear, we have developed multiple proprietary formulation technologies designed to deliver drug that is retained in the ear for an extended period of time following a single local administration, which we refer to as "sustained exposure." One of these technologies utilizes a thermosensitive polymer called poloxamer which transitions from a liquid to a gel at body temperature. The polymer vehicle is combined with drug microparticles to create a suspension that is retained in the ear for an extended period of time. This prolonged residence time provides high and sustained drug exposure.

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

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

We have a broad patent portfolio of approximately 37 issued patents and allowed patent applications and at least 45 pending patent applications in active prosecution covering our product, product candidates and indications as well as other potential applications of our drug delivery technologies in major markets around the world.

Competition

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

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

OTO-313

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

Hearing Loss Programs

There are no drugs currently approved by the FDA for the treatment of hearing loss. Oral steroids and repeat IT steroid injections are often used for the treatment of sudden sensorineural hearing loss (SSNHL), which is a rapidly emergent form of hearing loss. Hearing aids are used by a subset of patients with hearing loss and a limited number of patients with severe hearing loss are treated with cochlear implants. We are aware of a number of companies in clinical development with potential pharmaceutical treatments for various hearing loss indications,

including Altamira Therapeutics, which has reported negative results for a Phase 3 trial for AM-111 in SSNHL and terminated a second Phase 3 trial early, Fennec Pharmaceuticals, which has completed two Phase 3 trials and filed a New Drug Application with the FDA for PEDMARK™ in CIHL, Metarmor, which has conducted a Phase 3 trial with D-MET in noise-induced hearing loss (NIHL), Strekin AG, which is conducting a Phase 3 trial with STR001 in SSNHL, Sound Pharmaceuticals, which has completed a Phase 2 trial with SPI-1005 in patients with NIHL, is enrolling a Phase 2 trial for aminoglycoside-induced hearing loss (AIHL) prevention, and has stated plans to initiate a Phase 2 trial in CIHL, Audion Therapeutics, which has completed a Phase 2 trial with LY3056480 in patients with mild to moderate hearing loss, Sensorion, which has reported negative results for a Phase 2 trial with SENS-401 in SSNHL and has stated plans to initiate a Phase 2 trial in CIHL, Frequency Therapeutics, which has completed multiple Phase 1 studies and a Phase 2a trial of FX-322 in hearing loss patients with mixed results, and has initiated a Phase 2b trial in SSNHL and NIHL patients, Otologic Pharmaceutics, which has completed a Phase 1 trial with NHPN-010, Decibel Therapeutics, which has initiated a Phase 1b trial with DB-020 in CIHL, Spiral Therapeutics that has initiated a Phase 1 trial with LPT99 in SSNHL, and Pipeline Therapeutics that has completed a Phase 1/2 trial in SSNHL (results not announced). We are also aware of several companies conducting preclinical development for gene therapy programs targeting congenital hearing loss including Akouos, Inc., Decibel Therapeutics, BridgeBio Pharma, Inc. and Sensorion.

Third-Party Payor Coverage and Reimbursement

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

OTO-313 and OTO-413

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

Manufacturing

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

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

Poloxamer 407

The basis for the formulation of certain of our product candidates is P407, a thermosensitive polymer. We currently purchase P407 from a single supplier on a purchase-order basis under a supply agreement. Although P407 is available from other sources, changing suppliers could disrupt our supply chain. We believe that we can

effectively manage the risk of supply chain disruption by purchasing and storing quantities of P407 sufficient for our clinical requirements.

OTO-313

OTO-313 is a formulation containing gacyclidine. We currently purchase gacyclidine from a single supplier on a purchase-order basis and we do not have a long-term supply agreement. We currently use one third-party contract manufacturer to produce OTO-313 and are currently evaluating our supply chain to ensure support of our future clinical development requirements.

OTO-413

OTO-413 is a formulation containing BDNF. We currently purchase BDNF from a single supplier on a purchase-order basis and we do not have a long-term supply agreement. We are currently evaluating our supply chain to ensure support of our future clinical development requirements.

Intellectual Property

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

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

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

Our patent estate includes patents and applications with claims directed to our OTO-313, OTO-413, and other product candidates. Our patent estate also provides patents and applications with claims directed to a broad range of other active agents as potential future product candidates that are delivered using our proprietary technologies. Our patent estate, on a worldwide basis, includes approximately 37 issued patents and allowed patent applications, and at least 45 pending patent applications in active prosecution with claims relating to our OTO-313, OTO-413, other product candidates, future product candidates, manufacturing processes and alternative otic delivery technologies.

For OTO-313, we solely own a patent family directed to, among other things, the composition and therapeutic use of OTO-313. This family includes one issued U.S. patent and one pending U.S. application and pending applications in Australia, Canada, China, Europe, Hong Kong, Israel, India, Japan (allowed), and Korea. Any future U.S. and foreign patents issuing from those applications are expected to have an expiry date of June 2037. We also solely own a patent family directed to therapeutic use of OTO-313. Any future U.S. and foreign patents issuing from those applications are expected to have an expiry date of December 2041. In addition, we have licensed from

Durect, a patent family directed to the therapeutic use of OTO-313. This family includes one issued U.S. patent. The expiry date of the U.S. patent, without extension, is June 2024, and the patent is expected to be OB listable.

For OTO-413, we co-own a patent family with the Regents of the University of California (UC) directed to the composition and therapeutic use of OTO-413. Through an exclusive license agreement, we have acquired UC's rights in this patent family. Any future U.S. or foreign patents issuing from this patent family and directed to OTO-413 are expected to have an expiry date of April 2029. In addition, we solely own three patent families directed to certain aspects of the composition and therapeutic use of OTO-413. Any future U.S. or foreign patents issuing from those patent families and directed to OTO-413 are expected to have an expiry date of January 2039, January 2041 and December 2041, respectively.

In addition, we co-own eight other patent families with UC directed to a broad range of other active agents, including but not limited to, anti-TNF agents, auris pressure modulators, CNS modulators, cytotoxic agents, anti-apoptotic agents, bone-remodeling modulators, free radical modulators and ion channel modulators. As above, we have acquired, though an exclusive license, UC's rights in those co-owned families. Furthermore, to strengthen our protection against potential design-around, we solely own two patent families directed to alternative formulations. We will continue to pursue additional patent protection as well as take appropriate measures to obtain and maintain proprietary protection for our innovative technologies.

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

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

Our commercial success will also depend in part on not infringing upon the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, or our drugs or processes, obtain licenses or cease certain activities. Our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our future products may have a material adverse impact on us. If third parties prepare and file patent applications in the United States that also claim technology to which we have rights, we may have to participate in interference proceedings in the USPTO, to determine priority of invention. Although not involving issued U.S. patents covering OTIPRIO or any of our product candidates, on April 17, 2015, we filed a request for interference between one of our U.S. pending applications and a U.S. pending application that appears to be controlled by Auris Medical AG (Auris). On July 20, 2015, we received notice from the USPTO that the Patent Trial and Appeal Board

(PTAB) declared an interference between our pending application and the Auris patent (issued as U.S. Patent No. 9,066,865 on June 30, 2015). On January 26, 2017, the PTAB determined that all of our patent claims and all but one of the Auris patent claims are not patentable. In addition, the PTAB determined that the written description supporting Auris's single claim is as of Auris's filing date of 2014 rather than the 2005 date argued by Auris. This interference decision does not involve issued U.S. patents covering our product or product candidates. We filed a Notice of Appeal on March 27, 2017, in which we asked the Federal Circuit to reverse PTAB's decision that our claims are not patentable and that Auris's single claim is. On April 5, 2017, Auris filed a Notice of Cross-Appeal to ask the Federal Circuit to reverse PTAB's decision that Auris's other claims are not patentable. In August 2018, the Federal Circuit issued a final ruling in Otonomy's favor. 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. On September 15, 2020, the pending application was issued as U.S. Patent No. 10,772,828, which was assigned to ALK-Abelló, Inc. (ALK) in connection with the sale of assets related to OTIPRIO. We continue to monitor patent applications filed and being protected by Auris, in case we may need to consider similar or other actions. For more information, please see the section entitled "Risk Factors—Risks Related to Our Intellectual Property."

License and Other Agreements

The Regents of the University of California

In November 2008, we entered into an exclusive license agreement with UC that was subsequently amended in January 2010, June 2010, and November 2012. Under the license agreement, UC granted us an exclusive license under UC's rights to patents and applications that are co-developed and co-owned with us (see above regarding our patent estate) for the treatment of human otic diseases. As such, we have acquired the entire commercial rights in those patents and applications that cover OTO-413, and may apply to other product candidates we develop. Under the agreement, UC reserved the right to use the patents and applications for its and other nonprofit institutions' research and educational purposes.

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

Our financial obligations under the license agreement include development and regulatory milestone payments of up to $2.7 million per licensed product, of which $1.9 million has been paid for OTIPRIO, $0.8 million has been paid for OTIVIDEX, $0.4 million has been paid for OTO-413, and $0.1 million has been paid for OTO-311 (but such milestone payments are reduced by 75% for any orphan indication product), and a low single-digit royalty on net sales by us or our affiliates of licensed products. In addition, for each sublicense we grant we are obligated to pay UC a fixed percentage of all royalties as well as a sliding scale percentage of non-royalty sublicense fees received by us under such sublicense, with such percentage depending on the licensed product's stage of development when sublicensed to such third party. We have the right to offset a certain amount of third-party royalties, milestone fees or sublicense fees against the foregoing financial obligations, provided such third-party royalties or fees are paid by us in consideration for intellectual property rights necessary to commercialize a licensed product.

Unless earlier terminated, the agreement will continue in effect until expiration of the longest-lived patent licensed to us thereunder. UC may terminate the license agreement for our uncured breach, or if a claim challenging the validity of the licensed patents is filed by or on behalf of us. We have the right to terminate this agreement for any reason at any time upon prior notice to UC. The termination of our license agreement with UC may affect a portion of our patent portfolio for OTO-413, as well as certain other product candidates we may develop. For more information, please see the section entitled "Risk Factors—Risks Related to our Intellectual Property."

DURECT Corporation

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

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

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

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

Asset Transfer Agreement

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

Government Regulation

Government authorities in the United States (at the federal, state and local level) and in other countries extensively regulate, among other things, the research, development, testing, quality control, manufacture, packaging, storage, recordkeeping, approval, labeling, advertising, promotion, distribution, marketing, import and export of pharmaceutical products such as those we are developing. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations, require the expenditure of substantial time and financial resources. Our product candidates must be approved by the FDA before they may be legally marketed in the United States and by the appropriate foreign regulatory agency before they may be legally marketed in a foreign country. Generally, our

activities in other countries will be subject to regulation that is similar in nature and scope as that imposed in the United States, although there can be important differences. Additionally, some significant aspects of regulation in Europe are addressed in a centralized way, but country-specific regulation remains essential in many respects.

U.S. Drug Approval Process

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

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

Nonclinical Studies

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

Clinical Trials

Clinical trials involve the administration of the investigational new drug to patients under the supervision of qualified investigators in accordance with cGCP requirements, which include the requirement that all research patients provide their informed consent (assent, if applicable) in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it

commences at that institution. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health (NIH) for public dissemination on their ClinicalTrials.gov website.

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

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

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

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

As a result of the COVID-19 public health emergency, we may be required to develop and implement additional clinical trial policies and procedures designed to help protect subjects from the COVID-19 virus. For example, in March 2020, the FDA issued a guidance, which the FDA subsequently updated, on conducting clinical trials during the pandemic, which describes a number of considerations for sponsors of clinical trials impacted by the pandemic, including the requirement to include in the clinical trial report contingency measures implemented to manage the clinical trial, and any disruption of the clinical trial as a result of the COVID-19 pandemic, among others. The FDA has also published other COVID-19-related industry guidance, including updates to previous guidance, regarding Good Manufacturing Practices, remote interactive evaluations of drug manufacturing and bioresearch monitoring facilities, and drug product manufacturing and supply chain inspections, among others. The ultimate impact of the COVID-19 pandemic on our business operations is highly uncertain and subject to change and will depend on future developments, including new regulatory requirements and changes to existing regulations.

The NDA or BLA Approval Process

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

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

The FDA reviews an NDA or BLA to determine, among other things, whether the drug is safe and effective and the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity. The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA or BLA, the FDA typically will inspect the facility or facilities where the product is manufactured, which is not under the control of the product sponsor. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure compliance with cGCP.

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

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

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new products that meet certain criteria. Specifically, new products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. Unique to a Fast Track product, the FDA may consider for review sections of the NDA or BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA or BLA, the FDA agrees to accept sections and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA or BLA.

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

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

Post-Approval Requirements

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

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

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

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

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label, although doctors may prescribe drugs for off-label purposes.

The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

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

Hatch-Waxman Exclusivity

Market and data exclusivity provisions under the Federal Food, Drug, and Cosmetic Act (FFDCA) can delay the submission or the approval of certain applications for competing products. The FFDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a

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

New Legislation and Regulations

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

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any drug products for which we may obtain regulatory approval. Sales of any of our product candidates, if approved, will depend, in part, on the extent to which the costs of the products will be covered by third-party payors, including government health programs such as Medicare and Medicaid, commercial health insurers and managed care organizations. The process for determining whether a third-party payor will provide coverage for a drug product typically is separate from the process for setting the price of a drug product or for establishing the reimbursement rate that a payor will pay for the drug product once coverage is approved. Third-party payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the approved drugs for a particular indication.

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

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drugs have been a focus in this effort. Third-party payors are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost-effectiveness of drug products and medical services and questioning safety and efficacy. If these third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after FDA approval or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Adoption of

such controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals such as our drug product candidates and could adversely affect our net revenue and results.

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

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on drug pricing. Coverage policies, third-party reimbursement rates and drug pricing regulation may change at any time. In particular, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, which we collectively refer to as the Affordable Care Act (ACA), contains provisions that have the potential to substantially change healthcare delivery and financing, including impacting the profitability of drugs. Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA. For example, various portions of the ACA are currently undergoing legal and constitutional challenges in the Fifth Circuit Court and the United States Supreme Court. In June 2021 the U.S. Supreme Court held that Texas and other challengers had no legal standing to challenge the ACA, dismissing the case on procedural grounds without specifically ruling on the constitutionality of the ACA. Thus, the ACA will remain in effect in its current form. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how future challenges to the ACA and healthcare measures promulgated by the Biden administration will impact the ACA, our business, financial condition and results of operations. 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.

The ACA substantially changed the way healthcare is financed by both governmental and private insurers in the United States and significantly affected the pharmaceutical industry. The ACA includes provisions that may reduce the profitability of drug products through increased rebates for drugs reimbursed by Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. For example, the ACA revised the methodology by which rebates owed by manufacturers to the state and federal government for covered outpatient drugs under the Medicaid Drug Rebate Program, extended the Medicaid Drug Rebate Program to utilization of covered drugs dispensed to individuals enrolled in Medicaid managed care organizations and subjected manufacturers to new annual fees and taxes for certain branded prescription drugs. In 2020, under the Trump administration, the U.S. Department of Health and Human Services (HHS) issued various rules that were expected to impact, among others, price reductions from pharmaceutical manufacturers to plan sponsors under Part D, fee arrangements between pharmacy benefit managers and manufacturers, manufacturer price reporting requirements under the Medicaid Drug Rebate Program, including regulations that affect manufacturer-sponsored patient assistance programs subject to pharmacy benefit manager accumulator programs and Best Price reporting related to certain value-based purchasing arrangements. Multiple lawsuits have been brought against the HHS challenging various aspects of the rules implemented during the Trump administration. As a result, the Biden administration and HHS have delayed the implementation or published rules rescinding some of these Trump-era policies. Under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale

of products, which could have a material impact on our business. In addition, Congress is considering legislation that, if passed, could have significant impact on prices of prescription drugs covered by Medicare, including limitations on drug price increases and allowing Medicare to negotiate pricing for certain covered drug products. The impact of these regulations and any future healthcare measures and agency rules implemented by the Biden administration on us and the pharmaceutical industry as a whole is currently unknown.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, a number of states are considering or have recently enacted state drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such state laws once we begin commercialization after obtaining regulatory approval for any of our products.

Healthcare Law and Regulation

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescribing of any product candidates for which we may obtain marketing approval. Our business operations and arrangements with investigators, healthcare professionals, consultants, third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws. These laws may constrain the business or financial arrangements and relationships through which we research, manufacture, market, promote, sell and distribute our products that obtain marketing approval. Restrictions under applicable federal and state healthcare laws, include, but are not limited to, the following:

- the federal healthcare Anti-Kickback Statute prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal false claims laws and civil monetary penalties law impose penalties and provide for civil whistleblower or qui tam actions against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false or fraudulent or making a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) among other things, imposes criminal liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without proper written authorization;
- the federal Physician Payment Sunshine Act, created under the ACA, and implementing regulations, require applicable manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program to annually report to CMS, an agency within HHS, information related to payments and other transfers of value provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician healthcare professionals (such as physician assistants and nurse practitioners, among others) and teaching hospitals, as well as information regarding certain ownership and investment interests held by physicians and their immediate family members; and

- analogous state and foreign laws, such as state anti-kickback and false claims laws, that may apply to our business operations, including our sales or marketing arrangements, and claims involving healthcare items or services reimbursed by governmental third-party payors, and in some instances, also such claims reimbursed by non-governmental third-party payors, including private insurers.

Similar to the federal law, certain states also have adopted marketing and/or transparency laws relevant to manufacturers, some of which are broader in scope. Other states impose restrictions on manufacturers' marketing practices and require tracking and reporting of gifts, compensation, and other remuneration to healthcare professionals and entities. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. For instance, EU data protection law, in particular the EU General Data Protection Regulation (the GDPR), which became fully applicable in May 2018, includes, among other things, requirements for individuals' consent, restrictions on the processing of health data, notice obligations, restrictions for the transfer of personal data outside of the EU, security and confidentiality obligations, and significant fines in case of violation.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant administrative, civil, and/or criminal penalties, damages, fines, disgorgement, individual imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to administrative, civil, and/or criminal sanctions, including exclusions from government funded healthcare programs.

Foreign Regulation

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. The cost of establishing a regulatory compliance system for numerous varying jurisdictions can be very significant. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable foreign regulatory authorities before we can commence clinical trials or marketing of the product in foreign countries and jurisdictions. Although many of the issues discussed above with respect to the United States apply similarly in the context of the EU, the approval process varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

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

We may be subject to a variety of domestic and foreign anti-corruption laws with respect to our regulatory compliance efforts and operations. The U.S. Foreign Corrupt Practices Act, commonly known as the FCPA, is a criminal statute that prohibits an individual or business from paying, offering, promising or authorizing the provision of money (such as a bribe or kickback) or anything else of value (such as an improper gift, hospitality, or favor), directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision in order to assist the individual or business in obtaining, retaining, or directing business or other advantages (such as favorable regulatory rulings). The FCPA also obligates companies with securities listed in the United States to comply with certain accounting provisions. Those provisions require a company such as ours to (i) maintain books and records that accurately and fairly reflect all transactions, expenses, and asset dispositions, and (ii) devise and maintain an adequate system of internal accounting controls sufficient to provide reasonable assurances that transactions are properly authorized, executed and recorded. The FCPA is subject to broad interpretation by the U.S.

government. The past decade has seen a significant increase in enforcement activity. In addition to the FCPA, there are a number of other federal and state anti-corruption laws to which we may be subject, including, the U.S. domestic bribery statute contained in 18 USC § 201 (which prohibits bribing U.S. government officials) and the U.S. Travel Act (which in some instances addresses private-sector or commercial bribery both within and outside the United States). Also, a number of the countries in which we conduct activities have their own domestic and international anti-corruption laws, such as the UK Bribery Act 2010. There have been cases where companies have faced multi-jurisdictional liability under the FCPA and the anti-corruption laws of other countries for the same illegal act.

We can be held liable under the FCPA and other anti-corruption laws for the illegal activities of our employees, representatives, contractors, partners, agents, subsidiaries, or affiliates, even if we did not explicitly authorize such activity. Although we will seek to comply with anti-corruption laws, there can be no assurance that all of our employees, representatives, contractors, partners, agents, subsidiaries or affiliates will comply with these laws at all times. Noncompliance with these laws could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension and/or debarment from contracting with certain governments or other persons, the loss of export privileges, reputational harm, adverse media coverage, and other collateral consequences. In addition, our directors, officers, employees, and other representatives who engage in violations of the FCPA and certain other anti-corruption statutes may face imprisonment, fines, and penalties. If any subpoenas or investigations are launched, or governmental or other sanctions are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, results of operations and financial condition could be materially harmed. In addition, responding to any action will likely result in a materially significant diversion of management's attention and resources and significant defense costs and other professional fees. Enforcement actions and sanctions could further harm our business, results of operations, and financial condition.

Human Capital

As of December 31, 2021, we had 51 full-time employees. Of these employees, 39 were engaged in research and development activities, and 12 were engaged in general and administrative activities. None of our employees is represented by a labor union or covered by collective bargaining agreements, and we believe our employee relations are strong.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, and incentivizing our employees. The principal purposes of our equity and cash incentive plans are to attract, retain and reward personnel through the granting of stock-based and cash-based compensation awards, in order to increase stockholder value and the success of our company by motivating such individuals to remain focused on corporate objectives and perform to achieve our corporate objectives. Additionally, we believe that diversity, equity and inclusion improve employee experience and we are committed to furthering those principles with regard to our employees and business.

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 following directives from the State of California and the applicable local governments, and guidance from the CDC. Various safety protocols have been implemented and we are currently allowing employees who can remotely perform their essential functions to work from home as this was determined to be in the best interest of our employees and the communities in which we operate.

Channels for Disclosure of Information

Investors, the media and others should note that we may announce material information to the public through filings with the SEC, our website (www.otonomy.com), press releases, public conference calls and public webcasts. We encourage our investors, the media and others to follow the channels of disclosure listed above and review the information disclosed through any such channels as such information could be deemed to be material information. Please note that this list of channels of disclosure may be updated from time to time.

Corporate Information

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

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

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

Otonomy, the Otonomy logo, OTIVIDEX and other trademarks or service marks of Otonomy are the property of Otonomy. Other service marks, trademarks, and tradenames referred to in this Annual Report on Form 10-K are the property of their respective owners. Except as set forth above and solely for convenience, the trademarks and tradenames in this Annual Report on Form 10-K are generally referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Item 1A. RISK FACTORS

An investment in our securities involves a high degree of risk. You should carefully consider the specific factors discussed below, as well as all other information included in this Annual Report on Form 10-K, including our financial statements, the notes thereto and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations." If any of the following risks actually occurs, our business, financial condition, operating results, prospects and ability to accomplish our strategic objectives could be materially harmed. As a result, the trading price of our common stock could decline and you could lose all or part of your investment. 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 our securities.

Risk Factors Summary

Our business is subject to numerous risks and uncertainties, including those outside of our control, that could cause our actual results to be harmed, as fully described below. The principal factors and uncertainties that make investing in our company risky include, among others:

- We have a limited operating history and have incurred significant losses since our inception, and we anticipate that we will continue to incur losses for the foreseeable future, which makes it difficult to assess our future viability.
- We have not yet generated significant product revenue and may never become profitable.
- We will require additional financing to obtain regulatory approval for OTO-313, OTO-413, OTO-825 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.
- 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.
- We are dependent upon the advancement of our product candidates, such as OTO-313, OTO-413 and OTO-825, through clinical development to regulatory approval and commercialization.

- Clinical drug development involves a lengthy and expensive process with an uncertain outcome, results of earlier studies and trials may not be predictive of future trial results, and our clinical trials may fail to adequately demonstrate the safety and efficacy of our product candidates.
- We may be unable to obtain regulatory approval for our product candidates. The denial or delay of any such approval would delay commercialization and have a material adverse effect on our potential to generate revenue, our business and our results of operations.
- 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 candidates, such as OTO-313, OTO-413, and OTO-825, 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.
- Our product candidates, if approved, may 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.
- 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.
- 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.
- Our business and products are subject to extensive government regulation.

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 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 did not generate significant revenue, and we have decided not to pursue further development of our product candidate OTIVIDEX following a third Phase 3 trial that failed to achieve its primary endpoint. Our primary focus is currently on the advancement of OTO-313, which is currently in a Phase 2 trial for tinnitus, OTO-413, which is currently in a Phase 2a cohort for hearing loss, and OTO-825, which is a gene therapy for congenital hearing loss and is currently in IND-enabling studies. Additionally, we are conducting preclinical development of OTO-510 in otoprotection and OTO-6XX for severe hearing loss. As a result, we expect that it will be several years, if ever, before we receive approval to commercialize and generate revenue from sales of any of our current product candidates. Even if we succeed in receiving marketing approval for and commercializing one or more of our current product candidates, we expect that we will continue to incur substantial expenses in order to discover, develop and market additional product candidates.

We have recorded net losses of $51.2 million, $44.7 million and $44.7 million for the years ended December 31, 2021, 2020 and 2019, respectively. As of December 31, 2021, we had an accumulated deficit of $555.8 million. We continue to incur significant losses and significant research and development expenses related to our clinical trials and product development activities and other selling, general and administrative expenses. The net losses we incur may fluctuate significantly from quarter to quarter such that a period-to-period comparison of our results of operations may not be a good indication of our future performance, particularly since we expect our expenses to increase if and when our product candidates progress through clinical development as product candidates in later stages of clinical development generally have higher development costs than those in earlier

stages, primarily due to the increased size and duration of later-stage clinical trials. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our working capital, our ability to fund the development of our product candidates and our ability to achieve and maintain profitability and the performance of our stock.

We have not 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 product candidates, if approved. 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 did not generate significant revenue. In June 2020, we entered into a co-promotion agreement for OTIPRIO with ALK and, in May 2021, we sold our assets related to OTIPRIO to ALK.

We currently have no sales and marketing capabilities. Any failure or delay in developing our internal sales, marketing and distribution capabilities or entering promotional partnerships could adversely impact the commercialization of our product candidates, if approved. If we are not successful in commercializing our product candidates, if approved, 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 OTO-313, OTO-413, OTO-825 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-313 (formerly OTO-311) and OTO-413. In particular, conducting clinical trials for OTO-313 and OTO-413 and conducting IND-enabling activities for OTO-825 will require substantial funds. We have funded our operations primarily through the sale and issuance of common stock, convertible preferred stock and convertible notes. As of December 31, 2021, we had cash, cash equivalents and short-term investments of $77.4 million and an outstanding debt balance of $16.0 million, net of debt discounts. We believe that we will continue to expend substantial resources for the foreseeable future for the continued development of OTO-313, OTO-413, OTO-825 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 OTO-313, OTO-413, OTO-825 or any other product candidates;
- the cost of manufacturing our product candidates, if approved;
- the revenue generated by our product candidates, if approved;
- the cost of commercialization activities for 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;
- the degree and rate of market acceptance of any approved products;
- the emergence, approval, availability, perceived advantages, relative cost, relative safety and relative efficacy of other products or treatments;
- the expenses needed to attract and retain skilled personnel;
- the costs associated with being a public company;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims and other intellectual property rights, including litigation costs and the outcome of such litigation;
- the costs associated with legal and regulatory compliance;
- 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 (Cowen) 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 will act as sales agent or principal. As of December 31, 2021, $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 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, issued orders in March 2020 for all residents to remain at home, except as needed for essential activities as a result of the COVID-19 pandemic. In response to these safety protocols, we implemented work from home policies, and we are currently allowing employees who can remotely perform their essential functions to work from home. 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. As a result of the pandemic, enrollment of new patients in our OTIVIDEX trial was being managed on a site by site basis according to local conditions for a time and we temporarily paused new patient enrollment in our Phase 1/2 clinical trial of OTO-413 for a short period and then 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, our CROs, and/or clinical trial sites 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 which describes a number of considerations for sponsors of clinical trials impacted by the pandemic, including, among other requirements, the requirements to include in the clinical trial report contingency measures implemented to manage the clinical trial, any disruption of the clinical trial as a result of the COVID-19 pandemic, and analyses and corresponding discussions that address the impact of implemented contingency measures on the safety and efficacy results reported for the clinical trial. To the extent we (or our third party suppliers and manufacturers, CROs, clinical trial sites and vendors) are required to implement additional or to modify existing policies and procedures for our clinical studies and/or manufacturing functions, or if the pandemic significantly impacts recruitment of patients or the conduct of our clinical studies, our anticipated timelines for initiating or completing clinical studies and seeking regulatory approval may be substantially delayed, and we may incur additional costs. Also, to the extent FDA and other regulatory authorities experience any delays or limited resources in reviewing our regulatory applications or requests for meetings and/or guidance, and inspection of manufacturing facilities prior to regulatory approval due to the COVID-19 pandemic or other reasons, we may experience significant delays in our anticipated timelines for our clinical studies and/or seeking regulatory approvals, which could adversely affect our business.

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. We have experienced and may continue to experience longer lead times for certain raw materials and other supplies. Our third-party manufacturers may encounter disruptions in production and supply chain shortages may limit our access to raw materials and other supplies. If our third-party manufacturers or we encounter any such difficulties, our ability to manufacture or supply our product candidates for preclinical studies or clinical trials or, if approved, for commercial sale, could be delayed or halted entirely.

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 our clinical timelines, the development of our product candidates, and regulatory approval for our product candidates. For example, due to the COVID-19 pandemic various foreign and domestic inspections of facilities were largely placed on hold, although the FDA has been working to resume routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis. The FDA has developed a rating system to assist in determining when and where it is safest to conduct prioritized domestic inspections. In 2020 and 2021, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Although the FDA continues to ensure timely review of applications for medical products during the ongoing COVID-19 pandemic in line with its user fee performance goals and conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA Good Manufacturing Practices, the FDA may not be able to continue its current inspection pace, and review timelines could be extended if the FDA is unable to complete the required inspections during the review period. Regulatory authorities outside the U.S. may

adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. If a prolonged government shutdown or disruption occurs, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions and provide feedback on our clinical development plans, which could have a material adverse effect on our business and our anticipated timelines.

We may be required to develop and implement additional clinical trial policies and procedures designed to help protect subjects from the COVID-19 virus. For example, in March 2020, the FDA issued a guidance, which the FDA subsequently updated, on conducting clinical trials during the pandemic, which describes a number of considerations for sponsors of clinical trials impacted by the pandemic, including the requirement to include in the clinical trial report contingency measures implemented to manage the clinical trial, and any disruption of the clinical trial as a result of the COVID-19 pandemic, among others. Additional COVID-19 related guidance released by FDA include guidance addressing resuming normal drug and biologics manufacturing operations; manufacturing, supply chain, and inspections; and statistical considerations for clinical trials during the COVID-19 public health emergency. The FDA may issue additional guidance and policies that may materially impact our business and clinical development timelines. Changes to existing policies and regulations can increase our compliance costs or delay our clinical plans, including delays associated with complying with new requirements, impact on the operations of our contract manufacturers, our business, and our ability to obtain sufficient supplies for our clinical development on a timely basis.

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. To the extent that COVID-19 pandemic impacts our business in any way, it may also have the effect of heightening the impact of the risk factors outlined in this section.

Risks Related to Our Product Candidates, Business and Strategy

We are dependent upon the clinical, regulatory and commercial success of our product candidates.

Our business depends entirely on the successful discovery, development, regulatory approval and commercialization of product candidates. To date, we have obtained U.S. regulatory approval and launched a single product, OTIPRIO, but did not generate significant revenue, have no other products approved for commercial sale and do not anticipate generating any revenue from product sales of our current product candidates for the next several years, if ever. Our primary focus is currently on the advancement of OTO-313, which is currently in a Phase 2 trial for tinnitus, OTO-413, which is currently in a Phase 2a cohort for hearing loss, and OTO-825, which is a gene therapy for congenital hearing loss and is currently in IND-enabling studies. Additionally, we are conducting preclinical development of OTO-510 in otoprotection and OTO-6XX for severe hearing loss. Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve several objectives, including:

- successful and timely completion of nonclinical and clinical development of OTO-313, OTO-413, OTO-825, and our other product candidates;
- obtaining regulatory approval to commence clinical trials of our product candidates; establishing and maintaining relationships with CROs and clinical sites for the clinical development of OTO-313, OTO-413, OTO-825, and our other product candidates;
- the initiation and successful patient enrollment and completion of clinical trials on a timely basis; the use of, integrity of, patient compliance with, and adequacy of patient reported outcomes in our clinical trials;
- the efficacy and safety profiles that are satisfactory to the FDA or any comparable foreign regulatory authority for marketing approval;
- acceptable frequency and severity of adverse events in the clinical trials;

- timely receipt of marketing approvals from applicable regulatory authorities for any product candidates for which we successfully complete clinical development;
- complying with any required post-marketing approval commitments to applicable regulatory authorities; developing an efficient and scalable manufacturing process for our product candidates;
- establishing and maintaining commercially viable supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and meet the market demand for our product candidates, if approved;
- successful commercial launch following any marketing approval, including the development of a commercial infrastructure, whether in-house or with one or more collaborators;
- a continued acceptable safety profile following any marketing approval of our product candidates;
- commercial acceptance of our product candidates by patients, the medical community and third-party payors;
- identifying, assessing and developing new product candidates;
- obtaining, maintaining and expanding patent protection, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- protecting our rights in our intellectual property portfolio;
- defending against third-party infringement claims, if any;
- entering into, on favorable terms, any collaboration, licensing or other arrangements that may be necessary or desirable to develop, manufacture or commercialize our product candidates;
- obtaining coverage and adequate reimbursement by third-party payors for our products and patients' willingness to pay in the absence of such coverage and adequate reimbursement;
- obtaining additional funding to develop and potentially manufacture and commercialize our product candidates;
- addressing any competing therapies and technological and market developments;
- managing costs, including any unforeseen costs, that we may incur as a result of nonclinical study or clinical trial delays due to COVID-19 or other causes; and
- attracting, hiring and retaining qualified personnel including clinical, scientific, management and administrative personnel.

We may never be successful in achieving our objectives and, even if we do, may never generate revenue that is significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to maintain or further our research and development efforts, raise additional necessary capital, grow our business and continue our operations.

We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process or transferring that process to commercial partners, which may prevent us from completing our clinical trials or commercializing our product candidates on a timely or profitable basis, if at all. Changes in the manufacturing process or facilities will require further comparability analysis and approval by the FDA before implementation, which could delay our clinical trials and product candidate development, and could require additional clinical trials, including bridging studies, to demonstrate consistent and continued safety and efficacy.

Even if we successfully advance OTO-313, OTO-413 or OTO-825 through clinical development, or advance any other 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, OTO-825 or any other product candidate.

Risks Related to Our Business and Strategy

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

Clinical testing is expensive, 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 achieved its primary endpoint, while our AVERTS-1 Phase 3 clinical trial and third Phase 3 clinical trial did not, and we have since decided not to pursue any further development of this product candidate. 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 disclosed. 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 contract research organizations (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 and ensure compliance 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.

Our product candidates have previously been subject to clinical holds in the past, and we cannot assure you that our product candidates will not be subject to new clinical holds or significant delay in the future.

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

We may be unable to obtain regulatory approval for our product candidates. 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 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 candidates could be associated with side effects or adverse events which can vary in severity and frequency. Side effects or adverse events associated with the use of our product candidates may be observed at any time, including in clinical trials or once a product is commercialized, and any such side effects or adverse events may negatively affect our ability to obtain regulatory approval for our product candidates or market our product candidates, if approved. Side effects such as toxicity or other safety issues associated with the use of our 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 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 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, OTO-313, and OTO-413. 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 six other patients reported Grade 1 (mild) or Grade 2 (moderate) adverse events. If we are successful in commercializing our 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 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.

Our product candidates, OTO-313, OTO-413, OTO-825 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.

Our product candidates, if approved, may not achieve market acceptance among physicians and patients, and may not be commercially successful. For example, we launched OTIPRIO in March 2016, but we did not generate significant revenue from sales of OTIPRIO. Since then, we entered into co-promotion agreements with certain partners to support the promotion of OTIPRIO, including most recently with ALK in June 2020 for the promotion of OTIPRIO for the treatment of acute otitis externa (AOE), which was amended in October 2020 to include promotion

of OTIPRIO for use during tympanostomy tube placement (TTP) surgery. In May 2021, we sold our assets related to OTIPRIO to ALK.

There are currently no FDA-approved drug treatments for the indications we are pursuing for our product candidates. Our target 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. Our target indication for OTO-825 is the treatment of congenital hearing loss due to GJB2 mutation. A subset of patients with this condition are treated with cochlear implants. The commercial success of 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 any of our product candidates for its intended indication, 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 injecting the product;
- 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.

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 competitor drugs including off-label drug use by physicians to treat the indications for which we seek approval. We are aware that other companies, such as Akouos, Inc., Altamira Therapeutics Ltd. (formerly Auris Medical Holding AG), Audion Therapeutics, Autifony Therapeutics Ltd., BridgeBio Pharma, Inc., Decibel Therapeutics, Inc., Fennec Pharmaceuticals Inc., Frequency Therapeutics, Gateway Biotechnology, Otologic Pharmaceutics Inc., Pipeline Therapeutics, Sensorion SA, Sound Pharmaceuticals Inc., Spiral Therapeutics, and Strekin AG are developing potential products for the treatment of various otic indications, including tinnitus 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 or access to such data is impaired 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 product candidates.

We outsource the manufacture of our product candidates. We do not currently have the infrastructure or internal capability to manufacture supplies of our product candidates for use in development and commercialization. If we were to experience an unexpected loss of supply of our product candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, 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 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 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 or BLA 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 our product candidates or any other product candidates or products that we may develop. In addition, if the FDA does not accept these facilities for the manufacture of our product candidates or if it withdraws any such acceptance in the future, we 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 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 our product candidates, if approved.

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. For example, we have in the past manufactured batches of OTIPRIO that did not meet the appropriate specifications and could not be used. We may also manufacture an 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 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 for our product candidates including gacyclidine for OTO-313, poloxamer and BDNF for OTO-413 and an AAV-based gene therapy for OTO-825, from a small number of third-party suppliers. Because there are a limited number of suppliers for the raw materials that we use to manufacture our product candidates, we may need to engage alternate suppliers to prevent a possible disruption of the manufacture of the materials necessary to produce our product candidates for clinical trials. Our third-party manufacturers may encounter disruptions in production and supply chain shortages may limit our access to raw materials and other supplies. We do not have any control over the availability of raw materials. If we or our manufacturers are unable to purchase these raw materials on acceptable terms, at sufficient quality levels, or in adequate quantities, if at all, the development of OTO-313, OTO-413, OTO-825 or any other product candidates, would be delayed or there would be a shortage in supply, which would impair our ability to meet our development objectives and timelines for our product candidates or generate revenues from the sale of any approved products.

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

We are developing OTO-313 for the treatment of tinnitus, OTO-413 for the treatment of hearing loss, and OTO-825 for the treatment of congenital hearing loss due to GJB2 mutation. 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 candidates in the future, but we cannot predict when or if we will receive the regulatory approvals required to promote our 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 was approved for the treatment of pediatric patients with bilateral otitis media with effusion undergoing TTP surgery and for the treatment of AOE, and we could not promote its use in a manner that was inconsistent with the approved label. Although physicians are able to, in their independent medical judgment, use OTIPRIO for their patients in an off-label manner, such as for the treatment of other otic indications, if we had been found to have promoted such off-label uses, then we could have received warning letters and become subject to significant liability, which would have materially harmed 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. 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.

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.

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, as we did in the past for OTIPRIO.

There are no assurances that any future partnerships for our product candidates will be successful. 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 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. We intend to apply for a unique J Code for OTO-313, OTO-413 and OTO-825. We cannot assure you that J Codes will be issued for these product candidates, 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 OTO-313, OTO-413 and OTO-825, if approved, and the related potential revenue, may be significantly diminished. We cannot be certain that coverage and adequate reimbursement will be available for any of our product candidates, 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, 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 were extended to include payments and transfers of value made during the previous year to certain non-physician providers such as physician assistants and nurse practitioners, among others);
- 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. The U.S. Supreme Court heard oral arguments on the constitutionality of the ACA in November 2020 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. In June 2021, the U.S. Supreme Court held that Texas and other challengers had no legal standing to challenge the ACA, dismissing the case without specifically ruling on the constitutionality of the ACA. It is unclear how this Supreme Court decision, future litigation, or other efforts to repeal and replace the ACA, and healthcare measures of the current administration will impact the ACA and our business. 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.

Recently, there has been heightened governmental scrutiny over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several congressional inquiries and proposed and enacted federal and state legislation. In 2020, the U.S. Department of Health and Human Services (HHS) and CMS issued various rules in November and December of 2020 that were expected to impact, among others, price reductions from pharmaceutical manufacturers to plan sponsors under Part D, fee arrangements between pharmacy benefit managers and manufacturers, manufacturer price reporting requirements under the Medicaid Drug Rebate Program, including regulations that affect manufacturer-sponsored patient assistance programs subject to pharmacy benefit manager accumulator programs and Best Price reporting related to certain value-based purchasing arrangements. Multiple lawsuits have been brought against the HHS challenging various aspects of the rules implemented during the Trump administration. As a result, the Biden administration and HHS have delayed the implementation or published rules rescinding some of the policies issues under the Trump administration. Under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale of products, which could have a material impact on our business. In addition, Congress is considering legislation that, if passed, could have significant impact on prices of prescription drugs covered by Medicare, including limitations on drug price increases and allowing Medicare to negotiate pricing for certain covered drug products. The impact of these regulations and any future healthcare measures and agency rules implemented by the Biden administration on us and the pharmaceutical industry as a whole is currently unknown. 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 as our 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 clinical, scientific and commercial personnel, we may be unable to successfully develop and commercialize our product candidates.

Our success depends, in part, on our continued ability to attract, retain and motivate highly qualified management, clinical, scientific and commercial 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 ongoing and 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 any of our CROs, manufacturers, other contractors or consultants or potential future collaborators, may fail or suffer security or data privacy breaches or incidents or other unauthorized or improper access to, use of, or destruction of our proprietary or confidential data, employee data, or personal data, which could result in additional costs, loss of revenue, significant liabilities, harm to our brand and material disruption of our operations.

Despite the implementation of security measures in an effort to protect systems that store our information, given their size and complexity and the increasing amounts of information maintained and otherwise processed on our internal information technology systems, and those of our third-party CROs, other contractors (including sites performing our clinical trials) and consultants, these systems are potentially vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, natural disasters, terrorism, war and telecommunication and electrical failures, as well as security breaches and incidents from inadvertent or intentional actions by our employees, contractors, consultants, business partners, and/or other third parties, or from cyber-attacks by malicious third parties (including the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information), which may compromise our system infrastructure or lead to the loss, destruction, alteration, disclosure, or dissemination of, or damage or unauthorized access to, our data or data that is processed or maintained on our behalf, or other assets. For example, we have received phishing attacks, and companies have experienced an increase in phishing and social engineering attacks from third parties in connection with the COVID-19 pandemic, and the increase in remote working further increases security threats. If any disruption or security breach or incident were to result in any loss, destruction, unavailability, alteration, disclosure, or dissemination of, or damage to or unauthorized access, our applications, any other data processed or maintained on our behalf, or other assets, or for it to be believed or reported that any of these occurred, we could incur liability, financial harm and reputational damage and the development and commercialization of our product candidates could be delayed. We cannot assure you that our data protection efforts and our investment in information technology, or the efforts or investments of CROs, consultants or other third parties, will prevent significant breakdowns or breaches in systems or have prevented or will prevent other cyber incidents that cause loss, destruction, unavailability, alteration or dissemination of, or damage or unauthorized access to, our data or other data processed or maintained on our behalf or other assets that could have a material adverse effect upon our reputation, business, operations or financial condition. For example, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs and the development of our product candidates could be delayed. In addition, the loss of clinical trial data for our product candidates could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data. Furthermore, significant disruptions of our internal information technology systems or security breaches could result in the loss, misappropriation, and/or unauthorized access, use, or disclosure or dissemination of, or the prevention of access to, data (including trade secrets or other confidential information, intellectual property, proprietary business information, and personal information), which could result in financial, legal, business, and reputational harm to us. For example, any such event or any other security breach or incident that leads to loss, damage, or unauthorized access to, or use, alteration, or disclosure or

dissemination of, personal information, including personal information regarding our clinical trial subjects or employees, could harm our reputation directly, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information, which could result in significant legal and financial exposure and reputational damages that could potentially have an adverse effect on our business. To our knowledge, we have not experienced a material system failure, accident or security breach to date, nor are we aware of our CROs or other contractors experiencing any such material event negatively impacting ongoing trial data, but 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.

Notifications and follow-up actions related to a security breach or incident could impact our reputation and cause us to incur significant costs, including legal expenses and remediation costs. 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 lost data. We expect to incur significant costs in an effort to detect and prevent security incidents, and we may face increased costs and requirements to expend substantial resources in the event of an actual or perceived security breach. We also rely on third parties to manufacture our product candidates, and similar events relating to their computer systems could also have a material adverse effect on our business. If any disruption or security incident were to result in any disruption of our operations or loss, destruction, or alteration of, or damage or unauthorized access to, our data or other information that is processed or maintained on our behalf, or inappropriate disclosure or dissemination of any such information, we could be exposed to litigation and governmental investigations, the further development and commercialization of our product candidates could be delayed, and we could be subject to significant fines or penalties for any noncompliance with certain state, federal and/or international privacy and security laws.

Our insurance policies may not be adequate to compensate us for the potential losses arising from any such disruption in or, failure or security breach or incident of our systems or third-party systems where information important to our business operations or commercial development is stored or otherwise processed. In addition, such insurance may not be available to us in the future on economically reasonable terms, or at all. Further, our insurance may not cover all claims made against us and could have high deductibles in any event, and defending a suit, regardless of its merit, could be costly and divert management attention.

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. For example, in February 2016, the Financial Accounting Standards Board issued Accounting Standards Update No. 2016-02, *Leases (Topic 842)*, which aims to increase lease transparency and comparability among organizations. Further, we early adopted Accounting Standards Update No. 2019-12, *Income Taxes (Topic 740)—Simplifying the Accounting for Income Taxes*, effective January 1, 2020, which removes the exception to the incremental approach of intra-period tax allocation when there is a loss from continuing operations and income or gain from other items. 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 and data protection laws, and any laws regulating data security, 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 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. Additionally, our obligations to repay principal and interest on our indebtedness make us vulnerable to economic or market downturns. 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.

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. laws, 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, GDPR 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.

Inflation may adversely affect us by increasing our costs.

Recently, inflation has increased throughout the U.S. economy. Inflation can adversely affect us by increasing the costs of clinical trials and research, the development of our product candidates, administration and other costs of doing business. We may experience increases in the prices of labor and other costs of doing business. In an inflationary environment, cost increases may outpace our expectations, causing us to use our cash and other liquid assets faster than forecasted. If this happens, we may need to raise additional capital to fund our operations, which may not be available in sufficient amounts or on reasonable terms, if at all, sooner than expected.

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 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 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 candidates. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our product candidates, could be found to be infringed by our product candidates.

Third parties making claims against us for infringement or misappropriation of their intellectual property rights may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop our product candidates and commercialize our 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 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 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 candidate, the defendant could counterclaim that the patent covering our product candidate 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 candidates. They may also put our pending patent applications at risk of not issuing or issuing with limited and potentially inadequate scope to cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. Additionally, it is also possible that prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, may, nonetheless, ultimately be found by a court of law or an administrative panel to affect the validity or enforceability of a claim, for example if a priority claim is found to be improper. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could have a material adverse impact on our business.

Enforcing our or our 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 OTIPRIO 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. On September 15, 2020, the pending application was issued as U.S. Patent No. 10,772,828, which was assigned to ALK in connection with the sale of assets related to OTIPRIO.

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 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 OTO-413, as well as certain other product candidates we may develop. While we could still proceed with development and, if approved, commercialization of OTO-413 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 could reduce the breadth of our patent coverage for 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 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. Although we require all employees to enter into confidentiality and proprietary information agreements, 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 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 OTO-313, OTO-413, OTO-825 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 or BLA, as appropriate, 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 BLAs, or supplements to approved NDAs or BLAs.

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. Our product candidates have previously been subject to clinical holds in the past, and we cannot assure you that our product candidates will not be subject to new clinical holds or significant delay 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 OTO-313, OTO-413, OTO-825 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.

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 candidates, if approved, will be subject to extensive and ongoing regulatory requirements, including labeling and other restrictions and market withdrawal, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products. Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indications for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product. In addition, if any of our product candidates is approved, 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 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 information privacy and security laws regulating health, personal and other information. 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. In November 2020, California passed the California Privacy Rights Act (CPRA), which amends and expands the CCPA. The CCPA and the CPRA may impact our business activities and exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information. 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 EU, its member states, the UK, 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.

The GDPR introduces obligations around the transfer of personal data outside of the European Economic Area (EEA). There are several ways a company can compliantly transfer such information. On July 16, 2020, the Court of Justice of the European Union (CJEU) invalidated the U.S.-EU Privacy Shield framework that had been in place since 2016, which allowed companies like us to meet certain European legal requirements for the transfer of personal data from the EEA to the United States, and imposed additional obligations on companies when relying on the model clauses approved by the EU Commission. This CJEU decision may result in different EEA data protection regulators applying differing standards for, and require ad hoc verification of measures taken with respect to, certain personal data flows from the EEA to the U.S. The invalidation of the U.S.-EU Privacy Shield framework will require us to take additional steps to legitimize any personal data transfers that are impacted by this decision. This could result in increased costs of compliance and limitations on our business in the EU.

From the approval of OTIPRIO in 2015 until its sale to ALK in May of 2021, our operations were 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 (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician healthcare professionals (such as physician assistants and nurse practitioners, among others) and teaching hospitals, as well as information regarding certain ownership and investment interests held by physicians and their immediate family members.

If any of our business activities, including but not limited to our relationships with healthcare providers or payors, violate any of the aforementioned laws 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, 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 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.

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.

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

We may from time to time issue additional shares of common stock at a discount from the current trading price of our common stock. As a result, our stockholders would experience immediate dilution upon the purchase of any shares of our common stock sold at such discount. In addition, as opportunities present themselves, we may enter into financing or similar arrangements in the future, including the issuance of debt securities, preferred stock or common stock. In September 2018, our shelf registration statement on Form S-3 was declared effective by the SEC. Additionally, in August 2021, we filed with the SEC a new shelf registration statement on Form S-3 to replace the shelf registration statement filed in September 2018, pursuant to which we may offer debt securities, preferred stock, common stock and certain other securities from time to time up to a maximum aggregate amount of $150,000,000. In July 2020, we sold in a public offering 17,275,000 shares of our common stock, which includes the underwriters' full exercise of their option to purchase additional shares, and we sold pre-funded warrants to purchase 4,000,000

shares of our common stock. In April 2021, we sold in a public offering 8,298,890 shares of our common stock, which includes the underwriters' full exercise of their option to purchase additional shares, and we sold pre-funded warrants to purchase 7,111,110 shares of our common stock.

In August 2021, we filed a prospectus supplement in connection with an "at-the-market" offering pursuant to the terms of a sales agreement with Cowen, 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 experience further dilution by the exercise of the pre-funded warrants we have sold.

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

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

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

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

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

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

As of December 31, 2021, our executive officers, directors and current beneficial owners of 5% or more of our common stock, in aggregate, beneficially owned more than 52% 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. This risk is especially relevant for us because biotechnology companies have experienced significant stock price volatility in recent years and 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 and 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. 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. There is no guarantee that our capital stock will appreciate in value or even maintain the price at which you purchased your shares.

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

As of December 31, 2021, we had U.S. federal and state net operating loss carryforwards (NOLs) of approximately $436.7 million and $127.1 million, respectively. Of our federal NOLs, approximately $196.1 million were generated in a taxable year beginning after December 31, 2017, and therefore do not expire. Our remaining U.S. federal and state NOLs will expire in various years beginning in 2030, if not utilized. Under the legislation enacted in 2017, commonly referred to as the Tax Cuts and Jobs Act (the Tax Act), as modified by the CARES Act, the deductibility of our federal NOLs generated in taxable years beginning after December 31, 2017 will be limited to 80% of taxable income in taxable years beginning after December 31, 2020. As of December 31, 2021, we had federal and California research and development tax credit carryforwards of approximately $13.4 million and $6.5 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 post-change income and taxes may be limited or eliminated. 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. In addition, at the state level, there may be periods during which the use of net operating loss carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. For example, California imposed limits on the usability of California state net operating losses to offset taxable income in tax years beginning after 2019 and before 2023. We believe we have experienced ownership changes in the past and have reduced our deferred tax assets related to NOLs and research and development tax credit carryforwards accordingly. We are in the process of completing an analysis of ownership changes through December 31, 2021 which could result in substantial limitations in, or the elimination of, 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. 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." 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.

We have broad discretion in the use of the net proceeds from our public offerings, including our "at-the-market" offering, and may not use them effectively.

We have broad discretion as to how to spend and invest the proceeds from our public offerings, including our "at-the-market" offering with Cowen, and we may spend or invest these proceeds in a way with which our stockholders disagree. Accordingly, investors will need to rely on our judgment with respect to the use of these proceeds and these uses may not yield a favorable return to our stockholders. In addition, until the net proceeds are used, they may be placed in investments that do not produce significant income or that may lose value.

Item 1B. UNRESOLVED STAFF COMMENTS

None.

Item 2. PROPERTIES

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

Item 3. LEGAL PROCEEDINGS

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

Item 4. MINE SAFETY DISCLOSURE

Not applicable.

PART II

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

Market Information for Common Stock

Our common stock began trading on The NASDAQ Global Select Market under the symbol "OTIC" on August 13, 2014. Prior to that date, there was no public trading market for our common stock.

Holders of Record

On February 22, 2022, the closing sale price of our common stock on The NASDAQ Global Select Market was $2.02. As of February 22, 2022, there were approximately 17 holders of record of our common stock. The actual number of stockholders is greater than this number of holders of record and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust or by other entities.

Dividend Policy

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

Recent Sale of Unregistered Securities

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

Use of Proceeds

None.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

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

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

Overview

We are a biopharmaceutical company dedicated to the development of innovative therapeutics for neurotology. We pioneered the application of drug delivery technology to the ear and are utilizing that expertise and proprietary position to develop products that achieve sustained drug exposure from a single local administration. Our primary focus is currently on the advancement of three programs in our broad pipeline: OTO-313 in Phase 2 for tinnitus; OTO-413 in Phase 2a for hearing loss; and OTO-825, a gene therapy for congenital hearing loss, in investigational new drug (IND)-enabling activities. Additionally, we are conducting preclinical development of OTO-510 for otoprotection and OTO-6XX for severe hearing loss. We estimate, based on an external market report commissioned by us, that approximately 28 million people in the United States suffer from moderate to severe tinnitus or hearing loss.

OTO-313 is a sustained-exposure formulation of gacyclidine, a potent and selective NMDA receptor antagonist, in development for the treatment of tinnitus. In July 2020, we announced positive top-line results from a Phase 1/2 clinical trial of OTO-313 in patients with persistent tinnitus of at least moderate severity. We have completed enrollment in a Phase 2 clinical trial for OTO-313, with top-line results expected in mid-2022. We are also initiating clinical safety evaluations for higher and bilateral dosing of OTO-313, with top-line results expected in the second half of 2022. If positive, we expect these clinical data to support an End-of-Phase 2 meeting with the FDA and inform the design of the OTO-313 Phase 3 clinical program planned to start in the first half of 2023.

OTO-413 is a sustained-exposure formulation of BDNF in development for the treatment of hearing loss. In December 2020, we announced positive top-line results from a Phase 1/2 clinical trial of OTO-413 across multiple speech-in-noise hearing tests. We have completed enrollment in a Phase 2a cohort for OTO-413, with top-line results expected early in the second quarter of 2022. Additionally, we have initiated enrollment to evaluate higher dosing of OTO-413, with top-line results expected in the second half of 2022. Based on results from the Phase 2a cohort and higher-dose evaluation, we plan to initiate a full dose-ranging Phase 2 efficacy trial by the end of 2022.

OTO-825 is a gene therapy targeting mutations in the GJB2 gene, which is the most common cause of congenital hearing loss. Preclinical proof-of-concept results for OTO-825 demonstrate that a single administration of OTO-825 rescues hearing loss and cochlear damage in two preclinical models representing a range of hearing loss severity caused by GJB2 deficiency. We have completed a Pre-IND meeting with the FDA that provided guidance regarding nonclinical study design, manufacturing requirements and clinical trial considerations. Based on this feedback, we have initiated IND-enabling activities that we expect to support an IND filing in the first half of 2023.

OTO-510 is a product candidate in preclinical development for the prevention of cisplatin-induced hearing loss (CIHL), which routinely occurs in patients undergoing treatment with this chemotherapeutic agent. OTO-510 has demonstrated improved otoprotection in preclinical studies compared to other drug candidates in clinical development, and is being formulated to provide sustained exposure from a single intratympanic injection. The goal of the OTO-510 program is to preserve hearing without protecting the tumor.

Our OTO-6XX program is evaluating the treatment of severe hearing loss by repairing or regenerating auditory hair cells. In July 2020, we entered into an exclusive license agreement with Kyorin that provides us with exclusive worldwide rights to develop, manufacture and commercialize a novel compound from Kyorin for this program.

We have a limited operating history. Since our inception in 2008, we have devoted substantially all our efforts to developing and commercializing OTIPRIO, developing OTIVIDEX and our current product candidates, and providing general and administrative support for these operations. In July 2020, we sold in a public offering 17,275,000 shares of our common stock, which includes the underwriters' full exercise of their option to purchase additional shares, and we sold pre-funded warrants to purchase 4,000,000 shares of our common stock for $64.2 million in total net proceeds after deducting underwriting discounts and commissions and offering expenses. In April 2021, we sold in a public offering 8,298,890 shares of our common stock, which includes the underwriters' full exercise of their option to purchase additional shares, and we sold pre-funded warrants to purchase 7,111,110 shares of our common stock for $32.2 million in total net proceeds after deducting underwriting discounts and commissions and offering expenses. As of December 31, 2021, we had cash, cash equivalents and short-term investments of $77.4 million and an outstanding principal debt balance of $16.0 million.

We have never been profitable, and as of December 31, 2021, we had an accumulated deficit of $555.8 million. Our net losses were $51.2 million, $44.7 million and $44.7 million for the years ended December 31, 2021 2020 and 2019, respectively. Substantially all our net losses have resulted from research and development expenses related to our clinical trials and product development activities, commercialization expenses to launch OTIPRIO in the U.S. market, and other general and administrative expenses.

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

- conduct clinical development of OTO-313 and OTO-413, and conduct IND-enabling studies of OTO-825;
- conduct preclinical development of OTO-510 and OTO-6XX;
- contract to manufacture our product candidates;
- evaluate opportunities for development of additional product candidates;
- maintain and expand our intellectual property portfolio;
- hire additional staff as necessary to execute our product development plan; and
- operate as a public company.

We believe that our existing cash, cash equivalents and short-term investments will be sufficient to fund our operations for a period of at least twelve months from the date of this Annual Report on Form 10-K. When additional financing is required, we anticipate we will seek funding through public or private equity or debt financings or other sources, such as potential collaboration arrangements. We may not be able to raise capital on terms acceptable to us, or at all. Our failure to raise capital could have a negative impact on our financial condition and our ability to pursue our business strategies.

In November 2008, we entered into an exclusive license agreement with the Regents of the University of California (UC). Under the license agreement, UC granted us an exclusive license under their rights to patents and applications that are co-developed and co-owned with us for the treatment of human otic diseases. Our financial obligations under the license agreement include development and regulatory milestone payments of up to $2.7 million per licensed product, of which $1.9 million has been paid for OTIPRIO, $0.8 million has been paid for OTIVIDEX, $0.4 million has been paid for OTO-413, and $0.1 million has been paid for OTO-311 (but such milestone payments are reduced by 75% for any orphan indication product), and a low single-digit royalty on net sales by us or our affiliates of licensed products. In addition, for each sublicense we grant we are obligated to pay UC a fixed percentage of all royalties as well as a sliding-scale percentage of non-royalty sublicense fees received by us under such sublicense, with such percentage depending on the licensed product's stage of development when sublicensed to such third party. We have the right to offset a certain amount of third-party royalties, milestone fees or sublicense fees against the foregoing financial obligations, provided such third-party royalties or fees are paid by us in consideration for intellectual property rights necessary to commercialize a licensed product.

In April 2013, we entered into an exclusive license agreement with DURECT Corporation (Durect), as part of an asset transfer agreement between us and IncuMed LLC, an affiliate of the NeuroSystec Corporation. Under this license agreement, Durect granted us an exclusive, worldwide, royalty-bearing license under Durect's rights to certain patents and applications covering our OTO-313 product candidate, as well as certain related know-how. Under this license agreement and the asset transfer agreement, we are obligated to make one-time milestone payments of up to $7.5 million for the first licensed product. Upon commercializing a licensed product, we are obligated to pay Durect tiered, low single-digit royalties on annual net sales by us or our affiliates or sublicensees of the licensed products, and we have the right to offset a certain amount of third-party license fees or royalties against such royalty payments to Durect. In addition, each sublicense we grant to a third party is subject to payment to Durect of a low double-digit percentage of all non-royalty payments we receive under such sublicense. Additionally, we are also obligated to pay the Institut National de la Santé et de la Recherche Médicale (INSERM), on behalf of Durect, for a low single-digit royalty payment on net sales by us or our affiliates or sublicensees upon commercialization of the licensed product. The foregoing royalty payment obligation to Durect would continue on a product-by-product and country-by-country basis until expiration or determination of invalidity of the last valid claim within the licensed patents that cover the licensed product, and the payment obligation to INSERM would continue so long as Durect's license from INSERM remains in effect.

Given the unprecedented and evolving nature of the COVID-19 pandemic, including the rise of new variants, 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 sites' ability to enroll patients, among other activities. 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 policies in line with directives from the State of California and the applicable local governments, and guidance from the CDC. Various safety protocols have been implemented and we are currently allowing employees who can remotely perform their essential functions to work from home as this was determined to be in the best interest of our employees and the communities in which we operate.

Financial Operations Overview

Operating Expenses

Research and development expenses

Our research and development expenses primarily consist of costs associated with the nonclinical and clinical development of our product candidates.

Our research and development expenses include:

- employee-related expenses, including salaries, benefits, travel and stock-based compensation expense;
- external development expenses incurred under arrangements with third parties, such as fees paid to CROs in connection with nonclinical studies and clinical trials, costs of acquiring and evaluating clinical trial data such as investigator grants, patient screening fees, laboratory work and statistical compilation and analysis, and fees paid to consultants;
- costs to acquire, develop and manufacture clinical trial materials, including fees paid to contract manufacturers;
- payments related to licensed product candidates and technologies with no alternative future use;
- costs related to compliance with drug development regulatory requirements; and
- facilities expenses which include allocated expenses for amortization of ROU assets, depreciation and other overhead expenses, and direct costs for laboratory and other supplies.

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

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

	Years Ended December 31,		
	2021	2020	2019
Third-party development costs:			
OTIVIDEX	$ 423	$ 4,383	$ 7,709
OTO-313	10,995	1,527	2,951
OTO-413	2,196	2,385	4,557
Total third-party development costs	13,614	8,295	15,217
Other unallocated internal research and development costs	21,059	19,702	17,588
Total research and development costs	$ 34,673	$ 27,997	$ 32,805

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

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

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

- per patient trial costs;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- changes in regulatory and legal requirements for clinical trials;
- the length of time required to enroll eligible patients;
- the number of patients that participate in the trials;
- the number of doses that patients receive;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring or other studies requested by regulatory agencies;
- the duration of patient follow-up;

- the phase of development of the product candidate;
- the manufacturing process and complexity of, expiration of, and amount of the drug product required for the clinical trials;
- the efficacy and safety profile of the product candidate; and
- the impacts of COVID-19.

Selling, general and administrative expenses

Our selling, general and administrative expenses consist primarily of employee-related expenses, including salaries, benefits, travel and stock-based compensation expense, as well as other related costs for our employees and consultants in executive, administrative, finance and human resource functions. Other selling, general and administrative expenses include facility-related costs not otherwise included in research and development, costs associated with prosecuting and maintaining our patent portfolio and corporate legal expenses, costs required for public company activities and infrastructure necessary for the general conduct of our business, and OTIPRIO product support expenses and profit-sharing fees payable to our co-promotion partners, which are reduced by payments received from them.

We expect our selling, general and administrative expenses to be substantial as we support development of our product candidates, and as we incur ongoing expenses related to audit, legal, regulatory, and tax-related services associated with maintaining compliance with stock exchange listing and SEC requirements, directors' and officers' liability insurance premiums, and investor relations-related expenses.

Other Income (Expense)

Other income (expense) primarily consists of interest income earned on cash and cash equivalents and short-term investments and interest expense related to our long-term debt and finance leases.

Critical Accounting Policies and Significant Judgments and Estimates

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

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

Clinical Trial Expense Accruals

We estimate expenses resulting from our obligations under contracts with vendors, CROs and consultants and under clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts vary and may result in payment flows that do not match the periods over which materials or services are provided.

We record clinical trial expenses in the period in which services are performed and efforts are expended. We accrue for these expenses according to the progress of the trial as measured by patient progression and the timing of various aspects of the trial. We estimate accruals through financial models taking into account discussion with applicable personnel and outside service providers as to the progress of trials. During the course of a clinical trial, we may adjust our clinical accruals if actual results differ from our estimates. We estimate accrued expenses as of

each balance sheet date based on the facts and circumstances known at that time. Our clinical trial accruals are dependent upon accurate reporting by CROs and other third-party vendors. Although we do not expect our estimates to differ materially from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low for any particular period. For the years ended December 31, 2021, 2020 and 2019 there were no material adjustments to our prior period estimates of accrued expenses for clinical trials.

Stock-based Compensation

We recognize non-cash expense for the fair value of all stock options and other share-based awards. We use the Black-Scholes-Merton option valuation model to calculate the fair value of stock options, using the single-option award approach and straight-line attribution method. For stock option and restricted stock unit grants, we recognize the fair value as expense on a straight-line basis over the vesting period of each respective stock option or restricted stock unit, generally between two and four years.

Recent Accounting Pronouncements

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

Other Information

Net Operating Loss and Research and Development Tax Credit Carryforwards

As of December 31, 2021, we had U.S. federal and state NOLs of approximately $436.7 million and $127.1 million, respectively. Of our federal NOLs, approximately $196.1 million were generated in a taxable year beginning after December 31, 2017, and therefore do not expire. Our remaining U.S. federal and state NOLs will expire in various years beginning in 2030, if not utilized. Under the legislation enacted in 2017 commonly referred to as the Tax Cuts and Jobs Act (the Tax Act), as modified by the CARES Act, the deductibility of our federal NOLs generated in taxable years beginning after December 31, 2017 will be limited to 80% of taxable income in taxable years beginning after December 31, 2020. As of December 31, 2021, we had federal and California research and development tax credit carryforwards of approximately $13.4 million and $6.5 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 post-change income and taxes may be limited or eliminated. 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. In addition, at the state level, there may be periods during which the use of net operating loss carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. For example, California imposed limits on the usability of California state net operating losses to offset taxable income in tax years beginning after 2019 and before 2023. We believe we have experienced ownership changes in the past and have reduced our deferred tax assets related to NOLs and research and development tax credit carryforwards accordingly. We are in the process of completing an analysis of ownership changes through December 31, 2021 which could result in substantial limitations in, or the elimination of, 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. 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.

As of December 31, 2021, we had a full valuation allowance against our net deferred tax assets.

Reduced Reporting Requirements

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." Additionally, we intend to rely on certain exemptions and reduced reporting requirements available to us as a non-accelerated filer, including those relating to providing an auditor's attestation report on our system of internal control over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act.

Results of Operations

Comparison of the Years Ended December 31, 2021 and 2020

The following table sets forth the significant components of our results of operations for the years ended December 31, 2021 and 2020 (in thousands):

	Years Ended December 31,		
	2021	2020	Change
Research and development	$ 34,673	$ 27,997	$ 6,676
Selling, general and administrative	14,707	14,575	132
Interest income	43	326	(283)
Interest expense	1,599	1,570	29

Research and development expenses. The increase of $6.7 million in research and development expenses resulted from a number of activities including: (i) a $9.4 million net increase in OTO-313 clinical trial and development costs; (ii) a $1.2 million increase in facilities and other operating expenses mainly due to the impairment of OTIVIDEX manufacturing equipment. The increase in research and development expenses was offset by a $3.9 million decrease in OTIVIDEX costs due to discontinuation of development activities following completion of the Phase 3 clinical trial in early 2021.

Selling, general and administrative expenses. Selling, general and administrative expenses were consistent year-over-year.

Interest income. Interest income was consistent year-over-year.

Interest expense. Interest expense was consistent year-over-year.

Comparison of the Years Ended December 31, 2020 and 2019

Refer to "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations—Results of Operations" in our 2020 Annual Report on Form 10-K for a discussion of the results of operations for the year ended December 31, 2020 compared to the year ended December 31, 2019.

Liquidity and Capital Resources

We have incurred significant losses and negative cash flows from operations since our inception. As of December 31, 2021, we had an accumulated deficit of $555.8 million and we expect to continue to incur significant losses for the foreseeable future. We expect our research and development and selling, general and administrative expenses to continue to be substantial for the foreseeable future and, as a result, we will need additional capital to fund our operations, which we may obtain through one or more public or private equity or debt financings, or other sources such as potential collaboration arrangements. However, additional capital may not be available in sufficient amounts or on reasonable terms, if at all.

As of December 31, 2021, we had cash, cash equivalents and short-term investments of $77.4 million. We have principally financed our operations through sales and issuances of our equity securities, debt financing as well as private placements of redeemable convertible preferred stock and convertible notes. Our primary contractual obligations include our facility lease and our term loans.

The following table sets forth a summary of the primary sources and uses of cash for the years ended December 31, 2021, 2020 and 2019 (in thousands):

	Years Ended December 31,		
	2021	2020	2019
Net cash (used in) provided by:			
Operating activities	$ (42,418)	$ (38,874)	$ (36,925)
Investing activities	55,963	(20,215)	28,296
Financing activities	33,100	64,663	195
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 46,645	$ 5,574	$ (8,434)

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

Net cash used in operating activities was $42.4 million in 2021 compared to $38.9 million in 2020. The increase in the utilization of cash was primarily due to an increase in operating losses compared to the prior year period. Net cash used in operating activities was $38.9 million in 2020 compared to $36.9 million in 2019. The increase in the utilization of cash was primarily due to a decrease in accrued expenses compared to an increase in the prior year.

Investing activities. The primary source of cash from investing activities was from maturities of short-term investments and the primary use of cash from investing activities was for purchases of short-term investments and capital expenditures.

Net cash provided by investing activities was $56.0 million in 2021 compared to net cash used in investing activities of $20.2 million in 2020 and net cash provided by investing activities of $28.3 million in 2019. The increase in net cash provided by investing activities in 2021 compared to 2020 was primarily due to net maturities of short-term investments used to fund operations. The increase in net cash used in investing activities in 2020 compared to 2019 was primarily due to net purchases of short-term investments.

Financing activities. The primary sources of net cash provided by financing activities were net proceeds from the sale of our equity securities and net proceeds from debt.

Net cash provided by financing activities was $33.1 million in 2021 compared to $64.7 million in 2020 and $0.2 million in 2019. Net cash provided by financing activities in 2021 consisted of $32.2 million related to the issuance of common stock and pre-funded warrants, net proceeds of $0.7 million from a loan and $0.2 million in net proceeds for shares issued upon stock option exercises and under our employee stock purchase plan. Net cash provided by financing activities in 2020 consisted of $64.2 million related to the issuance of common stock and pre-funded warrants and $0.5 million in net proceeds for shares issued upon stock option exercises and under our employee stock purchase plan. Net cash provided by financing activities in 2019 consisted of $0.2 million in net proceeds for shares issued upon stock option exercises and under our employee stock purchase plan.

At-the-Market Offering Program

In August 2019, we entered into a sales agreement (Sales Agreement) with Cowen to sell shares of our common stock having aggregate sales proceeds of up to $40.0 million, from time to time, through an "at-the-market" equity offering program under which Cowen will act as sales agent or principal. Under the Sales Agreement, we set the parameters for the sale of shares, including the number or dollar value of shares to be issued, the time period during which sales are requested to be made, limitation on the number of shares that may be sold in any one trading day and any minimum price below which sales may not be made. The Sales Agreement provides that Cowen will be entitled to compensation for its services that will equal 3.0% of the gross sales price per share of all shares sold through Cowen under the Sales Agreement. The Sales Agreement shall automatically terminate upon the issuance and sale of placement shares equaling sales proceeds of $40.0 million and may be terminated earlier by

either us or Cowen upon five days' notice. We have no obligation to sell any shares under the Sales Agreement and may at any time suspend solicitation and offers under the Sales Agreement. In August 2021, we filed a prospectus supplement in connection with an "at-the-market" offering under which we may sell shares of common stock for up to an aggregate of $40.0 million, and entered into a superseding sales agreement with Cowen on terms substantially similar to the Sales Agreement. Through December 31, 2021, we have not sold any shares under the Sales Agreement.

Term Loans

Oxford Loans

On December 31, 2018 (the Closing Date), we entered into a Loan and Security Agreement with Oxford Finance LLC (the Loan Agreement). On June 2, 2021 (the New Closing Date), we entered into the Third Amendment to the Loan Agreement (the Third Amendment and together with the Loan Agreement, the Loan Agreements), which amends the Loan Agreement. The Third Amendment was accounted for as a modification. The Loan Agreement provides for a $15.0 million secured term loan credit facility (the Original Term Loan) and the Third Amendment provides for an additional $1.0 million term loan (the New Term Loan and together with the Original Term Loan, the Term Loans). The proceeds of the Term Loans may be used for working capital and general corporate purposes. We had the right to prepay the Original Term Loan in whole or in part at any time, subject to a prepayment fee of 1.00%. Under the Third Amendment, we have the right to prepay the Term Loans in whole or in part at any time, subject to a prepayment fee of 3.00% if prepaid on or prior to the first anniversary of the New Closing Date, 2.00% if prepaid after the first anniversary of the New Closing Date and on or prior to the second anniversary of the New Closing Date, and 1.00% thereafter. Amounts prepaid or repaid under the Term Loans may not be reborrowed. The Original Term Loan was fully funded on the Closing Date and the New Term Loan was fully funded on the New Closing Date. The Original Term Loan's maturity was extended under the Third Amendment from December 1, 2023 to April 1, 2026 (the Maturity Date), and the New Term Loan matures on the Maturity Date. We paid a facility fee of 0.75% of the Original Term Loan and customary closing fees on the Closing Date and customary closing fees in respect of the Third Amendment on the New Closing Date.

The Term Loans bear interest at a floating rate equal to the greater of 5.25% and the prime rate as reported in the Wall Street Journal from time to time, plus 3.75% (9.0% as of December 31, 2021, the minimum interest rate). Interest on the Term Loans is payable monthly in arrears. We were permitted to make interest-only payments on the Original Term Loan until February 1, 2022, followed by consecutive equal monthly payments of principal and interest in arrears through maturity on December 1, 2023. Under the Third Amendment, we are permitted to make interest-only payments on the Term Loans until June 1, 2023, followed by consecutive equal monthly payments of principal and interest in arrears through the Maturity Date. The Third Amendment also permits the interest-only period to be extended by an additional twelve months subject to the achievement of certain milestones. The outstanding principal amount of the Term Loans, together with accrued and unpaid interest, is due on the Maturity Date. The net outstanding balance of the Term Loans was $16.0 million as of December 31, 2021.

Upon repayment or acceleration of the Term Loans, a final payment fee equal to 4.00% of the aggregate original principal amount of the Term Loans is payable (the Final Payment Fee). The Final Payment Fee of $0.6 million, as well as the initial facility fee and all other direct fees and costs associated with the Loan Agreements, was recognized as a debt discount. The debt discount is amortized to interest expense over the term of the Loan Agreements using the effective interest method.

Our obligations under the Loan Agreements are secured by substantially all of our assets, excluding intellectual property and subject to certain other exceptions and limitations.

The Loan Agreements contain customary affirmative covenants, including covenants regarding compliance with applicable laws and regulations, reporting requirements, payment of taxes and other obligations, and maintenance of insurance. Further, subject to certain exceptions, the Loan Agreements contain customary negative covenants limiting our ability to, among other things, sell assets, allow a change of control to occur (if the Term Loans are not repaid), make acquisitions, incur debt, grant liens, make investments, pay dividends or repurchase stock. Upon the occurrence and during the continuance of an event of default, the lenders may declare all outstanding principal and accrued and unpaid interest under the Loan Agreements immediately due and payable, increase the applicable rate of interest by 5.00%, and exercise the other rights and remedies provided for under the

Loan Agreements and related loan documents. The events of default under the Loan Agreements include payment defaults, breaches of covenants or representations and warranties, material adverse changes, certain bankruptcy events, cross defaults with certain other indebtedness, and judgment defaults.

Funding Requirements

We expect to continue to incur significant losses for the foreseeable future as we: (i) develop and seek regulatory approvals for our product candidates OTO-313, OTO-413 and OTO-825; and (ii) work to develop OTO-510, OTO-6XX and additional product candidates through research and development programs. We are subject to all the risks incident in the development of new therapeutic products, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business.

We believe that our existing cash, cash equivalents and short-term investments will be sufficient to fund our operations for a period of at least twelve months from the date of this Annual Report on Form 10-K. When additional financing is required, we anticipate that we will seek funding through public or private equity or debt financings or other sources, such as potential collaboration arrangements. For example, in August 2021, we filed with the SEC a new shelf registration statement on Form S-3, pursuant to which we may offer debt securities, preferred stock, common stock and certain other securities from time to time up to a maximum aggregate amount of $150,000,000. In August 2021, we filed a prospectus supplement under such shelf registration statement in connection with an "at-the-market" offering under which we may sell shares of common stock for up to an aggregate of $40.0 million. Additional capital may not be available in sufficient amounts or on reasonable terms, if at all, and 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 we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates. If we raise additional funds through the issuance of additional debt or equity securities, it could result in dilution to our existing stockholders, increased fixed payment obligations and the existence of securities with rights that may be senior to those of our common stock. If we incur indebtedness, we could become subject to covenants that would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Any collaboration agreements we enter into may provide capital in the near-term but limit our potential cash flow and revenue in the future. Any of the foregoing could significantly harm our business, financial condition and prospects.

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

- the design, initiation, progress, size, timing, costs and results of nonclinical studies and clinical trials for our product candidates, including OTO-313, OTO-413 and OTO-825;

- the outcome, timing and cost of regulatory approvals by the FDA and comparable foreign regulatory authorities, including the potential for the FDA or comparable foreign regulatory authorities to require that we perform more studies than, or evaluate clinical endpoints other than, those that we currently expect;
- the revenue generated by our product candidates, if approved;
- the timing and costs associated with manufacturing our product candidates for clinical trials, nonclinical studies and for commercial sale;
- the cost of building and maintaining sales, marketing and distribution capabilities for any products for which we may receive regulatory approval and commercialize, including related facilities expansion costs;
- the number and characteristics of product candidates that we pursue;
- the potential acquisition and in-licensing of other technologies, products or assets;
- the extent to which we are required to pay milestone or other payments under our in-license agreements and the timing of such payments;
- the cost of obtaining, maintaining, defending and enforcing any patent claims and other intellectual property rights, including litigation costs and the outcome of such litigation;
- the cost associated with legal and regulatory compliance;
- our need to expand our development activities, including our need and ability to hire and adequately compensate additional employees;
- the potential impacts of the COVID-19 pandemic;
- the costs associated with being a public company;
- the effect of competing technological and market developments; and
- the cost of litigation, including potential patent litigation.

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

Item 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

As a "smaller reporting company" as defined in Rule 12b-2 of the Exchange Act, we are not required to provide the information required by this item.

Item 8. FINANCIAL STATEMENTS

Otonomy, Inc.

Index to Financial Statements

Report of Independent Registered Public Accounting Firm

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

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Otonomy, Inc. (the Company) as of December 31, 2021 and 2020, the related statements of operations, comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2021, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing separate opinions on the critical audit matter or on the account or disclosure to which it relates.

Clinical Trial Expense Accrual

Description of the Matter	As of December 31, 2021, the Company recorded $1.3 million for accrued clinical trial costs. As described in Note 2 of the Form 10-K, the Company records accruals for estimated costs of clinical trial activities, resulting from the Company's obligations under contracts with vendors, contract research organizations and consultants and under clinical site agreements in connection with conducting clinical trials. The Company accounts for these expenses according to the progress of the trial as measured by patient progression and the timing of various aspects of the trial. Estimated accruals are determined based on reviewing contractual terms and through communications with internal clinical personnel and external service providers including Contract Research Organizations ("CRO") as to the progress or state of its trials. Auditing management's accounting for accrued clinical trial expenses was especially challenging as calculating the liability for clinical trial activity includes determining the progress or stage of completion of the activities included in the individual clinical trial agreements based on internal and external information, and involves a high volume of data.
How We Addressed the Matter in Our Audit	To test the adequacy of the Company's clinical trial expense accruals, we performed audit procedures that included, amongst others, obtaining supporting evidence of the status of significant clinical trials based on communications with both internal and external clinical trial service providers. For instance, we attended internal clinical trial and project status meetings with accounting personnel and clinical project managers to corroborate the status of clinical trial activities. To verify the appropriate measurement of accrued clinical trial costs, we reviewed significant agreements, confirmed fees and status directly with the CRO, selected a sample of transactions to compare the recorded expense against related invoices and contracts, recalculated the clinical expense and accrual and tested a sample of payments made subsequent to year-end to evaluate the completeness of the clinical trial expense accruals.

/s/ Ernst & Young LLP

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

San Diego, California
February 28, 2022

Otonomy, Inc.

Balance Sheets
(in thousands, except share and per share data)

	December 31,	
	2021	2020
Assets		
Current assets:		
Cash and cash equivalents	$ 77,412	$ 30,767
Short-term investments	—	55,576
Prepaid and other current assets	3,056	2,372
Total current assets	80,468	88,715
Restricted cash	702	702
Property and equipment, net	1,771	2,766
Right-of-use assets	12,696	14,082
Total assets	$ 95,637	$ 106,265
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,090	$ 849
Accrued expenses	4,338	2,953
Accrued compensation	3,450	3,927
Leases, current	3,455	3,265
Total current liabilities	12,333	10,994
Long-term debt, net	15,997	15,158
Leases, net of current	12,400	13,847
Total liabilities	40,730	39,999
Commitments and Contingencies		
Stockholders' equity:		
Preferred stock, $0.001 par value, 10,000,000 shares authorized at December 31, 2021 and 2020; no shares issued or outstanding at December 31, 2021 and 2020	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized at December 31, 2021 and 2020; 56,732,474 and 48,318,970 shares issued and outstanding at December 31, 2021 and 2020, respectively	57	48
Additional paid-in capital	610,655	570,841
Accumulated other comprehensive income	—	1
Accumulated deficit	(555,805)	(504,624)
Total stockholders' equity	54,907	66,266
Total liabilities and stockholders' equity	$ 95,637	$ 106,265

See accompanying notes.

Otonomy, Inc.

Statements of Operations
(in thousands, except share and per share data)

	Years Ended December 31,		
	2021	2020	2019
Product sales, net	$ 125	$ 273	$ 600
Costs and operating expenses:			
Cost of product sales	370	1,188	912
Research and development	34,673	27,997	32,805
Selling, general and administrative	14,707	14,575	11,690
Total costs and operating expenses	49,750	43,760	45,407
Loss from operations	(49,625)	(43,487)	(44,807)
Other income (expense):			
Interest income	43	326	1,723
Interest expense	(1,599)	(1,570)	(1,591)
Total other (expense) income, net	(1,556)	(1,244)	132
Net loss	(51,181)	(44,731)	(44,675)
Net loss per share, basic and diluted	$ (0.81)	$ (1.10)	$ (1.45)
Weighted-average shares used to compute net loss per share, basic and diluted	63,441,330	40,845,844	30,726,786

See accompanying notes.

Otonomy, Inc.

Statements of Comprehensive Loss
(in thousands)

	Years Ended December 31,		
	2021	2020	2019
Net loss	$ (51,181)	$ (44,731)	$ (44,675)
Other comprehensive loss:			
Unrealized (loss) gain on available-for-sale securities	(1)	(10)	34
Comprehensive loss	$ (51,182)	$ (44,741)	$ (44,641)

See accompanying notes.

Otonomy, Inc.

Statements of Stockholders' Equity
(in thousands, except share data)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive (Loss) Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
lance at December 31, 2018	30,685,412	$ 31	$ 494,947	$ (23)	$ (415,218)	$ 79,7
Issuance of common stock upon exercise of stock options	2,912	—	5	—	—	
Issuance of common stock under employee stock purchase plan	125,887	—	242	—	—	2
Stock-based compensation expense	—	—	4,890	—	—	4,8
Net loss	—	—	—	—	(44,675)	(44,6
Unrealized gain on available-for-sale securities	—	—	—	34	—	
lance at December 31, 2019	30,814,211	31	500,084	11	(459,893)	40,2
Issuance of common stock and pre-funded warrants, net of issuance costs	17,275,000	17	64,170	—	—	64,1
Issuance of common stock upon exercise of stock options	92,035	—	206	—	—	2
Issuance of common stock under employee stock purchase plan	137,724	—	270	—	—	2
Stock-based compensation expense	—	—	6,111	—	—	6,1
Net loss	—	—	—	—	(44,731)	(44,7
Unrealized loss on available-for-sale securities	—	—	—	(10)	—	(
lance at December 31, 2020	48,318,970	48	570,841	1	(504,624)	66,2
Issuance of common stock and pre-funded warrants, net of issuance costs	8,298,890	9	32,198	—	—	32,2
Issuance of common stock upon exercise of stock options	2,836	—	6	—	—	
Issuance of common stock under employee stock purchase plan	111,778	—	213	—	—	2
Stock-based compensation expense	—	—	7,397	—	—	7,3
Net loss	—	—	—	—	(51,181)	(51,1
Unrealized loss on available-for-sale securities	—	—	—	(1)	—	
lance at December 31, 2021	56,732,474	$ 57	$ 610,655	$ —	$ (555,805)	$ 54,9

See accompanying notes.

Otonomy, Inc.,

Statements of Cash Flows
(in thousands)

	Years Ended December 31,		
	2021	2020	2019
Cash flows from operating activities:			
Net loss	$ (51,181)	$ (44,731)	$ (44,675)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	856	1,062	1,149
Stock-based compensation	7,397	6,111	4,890
Amortization of premiums (accretion of discounts) on short-term investments	85	(29)	(787)
Amortization of debt discount	172	191	189
Impairment of property and equipment	727	—	—
Changes in operating assets and liabilities:			
Prepaid and other assets	(1,564)	108	536
Accounts payable	276	(374)	127
Accrued expenses	1,459	(2,419)	1,656
Accrued compensation	(477)	1,334	(42)
Right-of-use assets and lease liabilities, net	(168)	(127)	32
Net cash used in operating activities	(42,418)	(38,874)	(36,925)
Cash flows from investing activities:			
Purchases of short-term investments	—	(68,581)	(85,004)
Maturities of short-term investments	55,490	48,500	114,000
Purchases of property and equipment	(295)	(134)	(700)
Proceeds from disposition	768	—	—
Net cash provided by (used in) investing activities	55,963	(20,215)	28,296
Cash flows from financing activities:			
Proceeds from issuance of common stock and pre-funded warrants, net of issuance costs	32,207	64,187	—
Proceeds from issuance of long-term debt, net of issuance costs	674	—	—
Proceeds from short-term debt	—	1,126	—
Principal payments on short-term debt	—	(1,126)	—
Proceeds from issuance of common stock under employee stock purchase plan	213	270	242
Proceeds from exercise of stock options	6	206	5
Payments of debt issuance costs	—	—	(52)
Net cash provided by financing activities	33,100	64,663	195
Net change in cash, cash equivalents and restricted cash	46,645	5,574	(8,434)
Cash, cash equivalents and restricted cash at beginning of period	31,469	25,895	34,329
Cash, cash equivalents and restricted cash at end of period	$ 78,114	$ 31,469	$ 25,895
Cash and cash equivalents at end of period	$ 77,412	$ 30,767	$ 25,194
Restricted cash at end of period	702	702	701
Cash, cash equivalents and restricted cash at end of period	$ 78,114	$ 31,469	$ 25,895
Supplemental cash flow information:			
Cash paid for interest	$ 1,422	$ 1,373	$ 1,394
Supplemental disclosure of non-cash investing and financing activities:			
Purchase of property and equipment in accounts payable and accrued expenses	$ 85	$ 67	$ 76

See accompanying notes.

Otonomy, Inc.,

Notes to Financial Statements

1. Description of Business and Basis of Presentation

Description of Business

Otonomy, Inc. (Otonomy or the Company) was incorporated in the state of Delaware on May 6, 2008. Otonomy is a biopharmaceutical company dedicated to the development of innovative therapeutics for neurotology. The Company pioneered the application of drug delivery technology to the ear and is utilizing that expertise and proprietary position to develop products that achieve sustained drug exposure from a single local administration. The Company's primary focus is currently on the advancement of three programs in its broad pipeline: OTO-313 in Phase 2 for tinnitus; OTO-413 in Phase 2a for hearing loss; and OTO-825, a gene therapy for congenital hearing loss, in investigational new drug (IND)-enabling activities. Additionally, the Company is conducting preclinical development of OTO-510 for otoprotection and OTO-6XX for severe hearing loss.

Basis of Presentation

The Company follows Accounting Standards Codification (ASC) Topic 205-40, *Presentation of Financial Statements—Going Concern*, which requires that management perform a two-step analysis over its ability to continue as a going concern. Management must first evaluate whether there are conditions and events that raise substantial doubt about the Company's ability to continue as a going concern and to meet its obligations as they become due within one year after the date that the financial statements are issued (step 1). If management concludes that substantial doubt is raised, management is also required to consider whether its plans alleviate that doubt (step 2).

The financial statements have been prepared assuming the Company will continue as a going concern, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. The Company has incurred operating losses and negative cash flows from operating activities since inception. As of December 31, 2021, the Company had cash, cash equivalents and short-term investments of $77.4 million, outstanding debt of $16.0 million and an accumulated deficit of $555.8 million. The Company anticipates that it will continue to incur net losses into the foreseeable future as it: (i) develops and seeks regulatory approvals for its product candidates; and (ii) works to develop additional product candidates through research and development programs. When additional financing is required, the Company anticipates that it will seek additional funding through future debt and/or equity financings or other sources, such as potential collaboration agreements. Additional capital may not be available in sufficient amounts or on reasonable terms, if at all. If the Company is not able to secure adequate additional funding, if or when necessary, the Company may be forced to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible, and/or suspend or curtail planned programs. Any of these actions could materially harm the Company's business, results of operations, and future prospects. The Company believes that its existing cash, cash equivalents and short-term investments will be sufficient to fund its operations for a period of at least twelve months from the date of this report.

2. Summary of Significant Accounting Policies

Use of Estimates

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

Segment Reporting

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

Concentrations of Credit Risk

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

Cash, Cash Equivalents and Restricted Cash

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

The Company's restricted cash consists of cash maintained in separate deposit accounts to secure a letter of credit issued by a bank to the landlord under a lease agreement for the Company's corporate headquarters.

Short-term Investments

From time to time, the Company carries short-term investments classified as available-for-sale debt securities at fair value as determined by prices for identical or similar securities at the balance sheet date. Short-term investments consist of Level 1 financial instruments in the fair value hierarchy (see Note 8 – *Fair Value*).

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

Fair Value of Financial Instruments

The Company's financial instruments include cash, cash equivalents, short-term investments, prepaid expenses and other assets, accounts payable, accrued expenses, accrued compensation and long-term debt. The carrying value of the Company's cash and cash equivalents, short-term investments, prepaid expenses and other current assets, other long-term assets, accounts payable, accrued expenses, and accrued compensation approximate fair value due to the short-term nature of these items. Based on Level 3 inputs and the borrowing rates currently available for loans with similar terms, the Company believes the fair value of long-term debt approximates its carrying value.

Property and Equipment, Net

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

useful lives of the assets. During the year ended December 31, 2021, the Company recorded an impairment to property and equipment, net of $0.7 million. No impairment was recorded during the years ended December 31, 2020 and 2019. Repairs and maintenance costs are charged to expense as incurred.

Impairment of Long-Lived Assets

The Company assesses the value of its long-lived assets for impairment on an annual basis and whenever events indicate that the carrying amount of such assets may not be recoverable. While the Company's current and historical operating losses and negative cash flows are indicators of impairment, the Company believes that future cash flows to be received support the carrying value of its long-lived assets. No impairment of long-lived assets was recorded during the years ended December 31, 2021, 2020 and 2019.

Right-of-Use Assets and Lease Liabilities

The Company has operating leases for its facility and certain equipment and finance leases for certain computer equipment. The Company determines if an arrangement is or contains a lease at each commencement date. Accounting Standards Codification (ASC) 842, *Leases* (ASC 842) establishes a right-of-use (ROU) model that requires a lessee to recognize an ROU asset and lease liability on the balance sheet for all leases with a term longer than 12 months. Accounting Standards Update (ASU) No. 2016-02, *Leases* (ASU 2016-02) provides a number of optional practical expedients and accounting policy elections. The Company elected the package of practical expedients requiring no reassessment of whether any expired or existing contracts are or contain leases, the lease classification of any expired or existing leases, or initial direct costs for any existing leases.

Operating leases are included in ROU assets, Leases, current, and Leases, net of current on the balance sheets. Finance leases are included in Property and equipment, Leases, current, and Leases, net of current on the balance sheets. The Company has elected a policy not to recognize short-term leases (one year or less) on the balance sheets. ROU assets and operating lease liabilities are recognized based on the present value of future minimum lease payments over the lease term at the commencement date. When the implicit rate of the lease is not provided or cannot be determined, the Company uses a collateralized incremental borrowing rate based on the information available at the commencement date, including lease term, in determining the present value of future payments. The Company considers payments for common area maintenance, real estate taxes and management fees to be variable non-lease components, which are expensed as incurred. Lease terms may include options to extend or terminate the lease when it is reasonably certain the Company will exercise that option. Lease expense for minimum lease payments is recognized on a straight-line basis over the lease term.

Clinical Trial Expense Accruals

The Company estimates expenses resulting from its obligations under contracts with vendors, contract research organizations (CROs) and consultants and under clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts vary and may result in payment flows that do not match the periods over which materials or services are provided.

The Company records clinical trial expenses in the period in which services are performed and efforts are expended. The Company accrues for these expenses according to the progress of the trial as measured by patient progression and the timing of various aspects of the trial. The Company estimates accruals through financial models taking into account discussion with applicable personnel and outside service providers as to the progress of trials. During the course of a clinical trial, the Company may adjust its clinical accruals if actual results differ from its estimates.

Collaborative Arrangements

The Company has entered into co-promotion agreements and research agreements that fall under the scope of ASC Topic 808, *Collaborative Arrangements* (ASC 808).

Co-promotion agreements can include payments and reimbursements for a proportion of product support expenses to the Company and profit sharing payments by the Company. Payments to or by the Company are recognized in selling, general and administrative expenses in the statements of operations.

Research agreements can include reimbursements to or by the Company, which are recognized in research and development expenses in the statements of operations.

License Fees

The Company expenses amounts paid to acquire licenses associated with products under development when the ultimate recoverability of the amounts paid is uncertain, and the technology has no alternative future use when acquired. Acquisitions of technology licenses are charged to expense or capitalized based upon management's assessment regarding the ultimate recoverability of the amounts paid and the potential for alternative future use. The Company has determined that technological feasibility for its product candidates would be reached when the requisite regulatory approvals are obtained to make the product available for sale.

Research and Development

Research and development expenses include the costs associated with the Company's research and development activities, including salaries, benefits, stock-based compensation expense and occupancy costs. Also included in research and development expenses are third-party costs incurred in conjunction with contract manufacturing for the Company's research and development programs and clinical trials, including the cost of clinical trial drug supply, costs incurred by CROs and regulatory expenses. Research and development costs are expensed as incurred.

Selling, General and Administrative

Selling, general and administrative expenses include the costs associated with the Company's executive, administrative, finance and human resource functions including salaries, benefits, stock-based compensation expense and occupancy costs. Other selling, general and administrative expenses include costs associated with prosecuting and maintaining the Company's patent portfolio, corporate legal expenses, costs required for public company activities and infrastructure necessary for the general conduct of the Company's business. The Company's selling, general and administrative expenses also include OTIPRIO product support expenses, and profit-sharing fees payable to the Company's partners, which are reduced by payments received from the Company's partners under its co-promotion agreements.

Stock-Based Compensation

The Company accounts for stock-based compensation expense related to stock options and employee stock purchase plan (ESPP) rights by estimating the fair value on the date of grant using the Black-Scholes-Merton option pricing model, while market price of the Company's common stock at the date of grant is used for restricted stock unit awards. Forfeitures are recognized as incurred. For awards subject to time-based vesting conditions, stock-based compensation expense is recognized using the straight-line method. For performance-based awards to employees, (i) the fair value of the award is determined on the grant date, (ii) the Company assesses the probability of the individual performance milestones under the award being achieved and (iii) the fair value of the shares subject to the milestone is expensed over the implicit service period commencing once management believes the performance criteria is probable of being met.

Income Taxes

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

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

Comprehensive Loss

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

Net Loss Per Share

Basic net loss per common share is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of common shares outstanding during the period, without consideration for potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders by the weighted-average number of common shares and potentially dilutive securities outstanding for the period determined using the treasury-stock and if-converted methods. For purposes of the diluted net loss per share calculation, potentially dilutive securities are excluded from the calculation of diluted net loss per share because their effect would be anti-dilutive and therefore, basic and diluted net loss per share were the same for all periods presented.

As of December 31, 2021, potentially dilutive securities excluded from the calculation of diluted net loss per share consist of outstanding options to purchase 11,707,568 shares of the Company's common stock and 1,650,250 unvested restricted stock units. As of December 31, 2020 and 2019, potentially dilutive securities excluded from the calculation of diluted net loss per share consist of outstanding options to purchase 9,842,744 and 7,495,129 shares of the Company's common stock, respectively.

Risks and Uncertainties Related to COVID-19

In March 2020, the World Health Organization declared COVID-19 a global pandemic. The COVID-19 pandemic could pose significant risks to the Company's business; however, the ultimate impact of the pandemic is highly uncertain.

Given the unprecedented and evolving nature of the COVID-19 pandemic, including the rise of new variants, there continues to be significant uncertainty about the progression and ultimate impact of the pandemic on the Company's operations. The Company has taken steps to mitigate the impact of the COVID-19 pandemic on its clinical trials, including developing processes to ensure the integrity of data collection from enrolled patients and supporting sites' ability to enroll patients, among other activities. Nonetheless the Company does not know the full extent of potential future delays or impacts on its business operations, its preclinical programs and clinical trials, healthcare systems, its 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, the Company has taken steps to protect the health and safety of its employees and community by following directives from the State of California and the applicable local governments, and guidance from the U.S. Centers for Disease Control and Prevention (CDC). Various safety protocols have been implemented and the Company is currently allowing employees who can remotely perform their essential functions to work from home.

Recent Accounting Pronouncements

Not Yet Adopted

In June 2016, ASU No. 2016-13, *Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* (ASU 2016-13) was issued, as amended. ASU 2016-13 introduces the current expected credit loss model, which will require an entity to measure credit losses for certain financial instruments and financial assets. ASU 2016-13 will also apply to receivables arising from revenue transactions such as accounts receivable. ASU 2016-13 is effective for the Company beginning January 1, 2023. The Company does not expect the adoption of ASU 2016-13 to have a material effect on its financial position, results of operations or cash flows.

Recently Adopted

Effective January 1, 2021, the Company early adopted ASU No. 2020-06, *Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40)* (ASU 2020-06). ASU 2020-06 simplifies the derivative scope exception guidance pertaining to equity classification of contracts in an entity's own equity. ASU 2020-06 amends the diluted earnings per share guidance, including the requirement to use the if-converted method for all convertible instruments. There was no cumulative effect to be recognized in connection with the early adoption of ASU 2020-06 and the adoption did not have a material impact on the Company's financial statements or disclosures.

3. Available-for-Sale Securities

The Company invests in available-for-sale debt securities consisting of money market funds, certificates of deposit, U.S. Treasury securities and U.S. government sponsored enterprise securities. Available-for-sale debt securities are classified as part of either cash and cash equivalents or short-term investments in the balance sheets. Available-for-sale debt securities with maturities of three months or less from the date of purchase have been classified as cash equivalents, and were $71.5 million and $23.3 million as of December 31, 2021 and 2020, respectively.

The Company held no available-for-sale debt securities with maturities of more than three months from the date of purchase as of December 31, 2021. Available-for-sale debt securities with maturities of more than three months from the date of purchase as of December 31, 2020 have been classified as short-term investments, and were as follows (in thousands):

	Amortized Cost	Unrealized Gains	Unrealized Losses	Market Value
December 31, 2020:				
U.S. Treasury securities	$ 55,085	$ 2	$ (1)	$ 55,086
Certificates of deposit	490	—	—	490
	$ 55,575	$ 2	$ (1)	$ 55,576

As of December 31, 2021, the Company had no securities in a gross unrealized loss position. At each reporting date, the Company performs an evaluation of impairment to determine if any unrealized losses are other-than-temporary. Factors considered in determining whether a loss is other-than-temporary include the length of time and extent to which fair value has been less than the cost basis, the financial condition of the issuer, and the Company's intent and ability to hold the investment until recovery of its amortized cost basis. The Company intends, and has the ability, to hold any investments in unrealized loss positions until their amortized cost basis has been recovered. The Company determined there were no other-than-temporary declines in the value of any available-for-sale securities as of December 31, 2021. All the Company's available-for-sale debt securities mature within one year.

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

4. Balance Sheet Details

Property and Equipment, Net

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

	December 31,	
	2021	2020
Laboratory equipment	$ 4,252	$ 4,265
Manufacturing equipment	82	1,075
Computer equipment and software	1,488	989
Leasehold improvements	822	768
Office furniture	1,507	1,548
	8,151	8,645
Less: accumulated depreciation	(6,380)	(5,879)
Total	$ 1,771	$ 2,766

Depreciation expense was $0.9 million, $1.1 million and $1.1 million for the years ended December 31, 2021, 2020 and 2019, respectively.

Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31,	
	2021	2020
Accrued clinical trial costs	$ 1,279	$ 1,477
Accrued other	3,059	1,476
Total	$ 4,338	$ 2,953

5. Commitments and Contingencies

Operating Leases

In December 2016, the Company moved into its current headquarters location in San Diego, California. The lease commenced in December 2016 and has an initial term of 130 months, with an option by the Company to extend the lease term for an additional five years. The Company has the right to terminate the lease at the end of the 94th month of the lease term if it is acquired by a third party and pays an early termination fee. The Company is responsible for payment of taxes and operating expenses for the building, in addition to monthly base rent in the initial amount of approximately $232,000, with 3% annual increases, which monthly base rent was abated for the first ten months of the lease term. The total estimated base rent payments over the life of the lease are estimated to be approximately $32.7 million. Upon execution of the lease in May 2015, the Company provided a security deposit in the form of a letter of credit in the amount of approximately $0.7 million. Cash collateralizing the letter of credit is classified as noncurrent restricted cash on the balance sheets. The Company has determined that the lease is an operating lease for accounting purposes.

Intellectual Property Licenses

The Company has acquired exclusive rights to develop patented rights, information rights and related know-how for OTO-311, OTO-313, OTO-413 and OTIVIDEX and potential future product candidates under licensing agreements with third parties. The licensing rights obligate the Company to make payments to the licensors for license fees, milestones and royalties. The Company is also responsible for patent prosecution costs, in the event such costs are incurred.

The Company may be obligated to make additional milestone payments under the Company's intellectual property license agreements covering OTO-313 and OTO-413 as follows (in thousands):

Development	$ 1,250
Regulatory	7,675
Commercialization	1,000
Total	$ 9,925

The table above includes a potential milestone payment of $0.3 million under one of the Company's license agreements payable if the Company initiates a Phase 2 trial for OTO-413 in 2022.

In July 2020, the Company entered into an exclusive license agreement to develop, manufacture and commercialize a novel compound as a potential treatment, OTO-6XX, for severe hearing loss. Under the terms of the agreement, the Company acquired worldwide rights to the compound for an upfront payment of $0.5 million with an additional $0.5 million due upon demonstration of preclinical efficacy. If the Company advances a product containing the compound into full development, the Company may be obligated to make payments for development and commercial milestones and pay a royalty on worldwide net sales. The license agreement was accounted for as an asset acquisition and the upfront cash payment of $0.5 million was expensed to research and development during the year ended December 31, 2020 as there is no future alternative use for the assets.

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

	Years Ended December 31,		
	2021	2020	2019
License and other fees	$ —	$ 500	$ —
Milestone fees	—	250	100
Total license and related fees	$ —	$ 750	$ 100

Other Royalty Arrangements

In October 2014, the Company entered into an exclusive license agreement with Ipsen that enables the Company to use clinical and nonclinical gacyclidine data generated by Ipsen to support worldwide development and regulatory filings for OTO-313. Under this license agreement, the Company is obligated to pay Ipsen low single-digit royalties on annual net sales of OTO-313 by the Company or its affiliates or sublicensees, up to a maximum cumulative royalty totaling $10.0 million.

Litigation

From time to time, the Company may be involved in various lawsuits, legal proceedings, or claims that arise in the ordinary course of business. Management believes there are no claims or actions pending against the Company as of December 31, 2021 which will have, individually or in the aggregate, a material adverse effect on its business, liquidity, financial position, or results of operations. Litigation, however, is subject to inherent uncertainties, and an adverse result in these or other matters may arise from time to time that may harm the Company's business.

6. Debt

Term Loans

On December 31, 2018 (the Closing Date), the Company entered into a Loan and Security Agreement (the Loan Agreement), among the Company, Oxford Finance LLC, as collateral agent, and the lenders party thereto from time to time. On June 2, 2021 (the New Closing Date), the Company entered into the Third Amendment to the Loan Agreement (the Third Amendment and together with the Loan Agreement, the Loan Agreements), which amends the Loan Agreement. The Third Amendment was accounted for as a modification.

The Loan Agreement provides for a $15.0 million secured term loan credit facility (the Original Term Loan) and the Third Amendment provides for an additional $1.0 million term loan (the New Term Loan and together with the Original Term Loan, the Term Loans). The proceeds of the Term Loans may be used for working capital and general corporate purposes. The Company had the right to prepay the Original Term Loan in whole or in part at any time, subject to a prepayment fee of 1.00%. Under the Third Amendment, the Company has the right to prepay the Term Loans in whole or in part at any time, subject to a prepayment fee of 3.00% if prepaid on or prior to the first anniversary of the New Closing Date, 2.00% if prepaid after the first anniversary of the New Closing Date and on or prior to the second anniversary of the New Closing Date, and 1.00% thereafter. Amounts prepaid or repaid under the Term Loans may not be reborrowed. The Original Term Loan was fully funded on the Closing Date and the New Term Loan was fully funded on the New Closing Date. The Original Term Loan's maturity was extended under the Third Amendment from December 1, 2023 to April 1, 2026 (the Maturity Date), and the New Term Loan matures on the Maturity Date. The Company paid a facility fee of 0.75% of the Original Term Loan and customary closing fees on the Closing Date and customary closing fees in respect of the Third Amendment on the New Closing Date.

The Term Loans bear interest at a floating rate equal to the greater of 5.25% and the prime rate as reported in the Wall Street Journal from time to time, plus 3.75% (9.0% as of December 31, 2021, the minimum interest rate). Interest on the Term Loans is payable monthly in arrears. The Company was permitted to make interest-only payments on the Original Term Loan until February 1, 2022, followed by consecutive equal monthly payments of principal and interest in arrears through maturity on December 1, 2023. Under the Third Amendment, the Company is permitted to make interest-only payments on the Term Loans until June 1, 2023, followed by consecutive equal monthly payments of principal and interest in arrears through the Maturity Date. The Third Amendment also permits the interest-only period to be extended by an additional twelve months subject to the achievement of certain milestones. The outstanding principal amount of the Term Loans, together with accrued and unpaid interest, is due on the Maturity Date.

Upon repayment or acceleration of the Term Loans, a final payment fee equal to 4.00% of the aggregate original principal amount of the Term Loans is payable (the Final Payment Fee). The Final Payment Fee of $0.6 million, as well as the initial facility fee and all other direct fees and costs associated with the Loan Agreements, was recognized as a debt discount. The debt discount is being amortized to interest expense over the term of the Loan Agreements using the effective interest method.

The Company's obligations under the Loan Agreements are secured by substantially all its assets, excluding intellectual property and subject to certain other exceptions and limitations.

The Loan Agreements contain customary affirmative covenants, including covenants regarding compliance with applicable laws and regulations, reporting requirements, payment of taxes and other obligations, and maintenance of insurance. Further, subject to certain exceptions, the Loan Agreements contain customary negative covenants limiting the ability of the Company to, among other things, sell assets, allow a change of control to occur (if the Term Loans are not repaid), make acquisitions, incur debt, grant liens, make investments, pay dividends or repurchase stock. The Company has maintained compliance with all such covenants to date. Upon the occurrence and during the continuance of an event of default, the lenders may declare all outstanding principal and accrued and unpaid interest under the Loan Agreements immediately due and payable, increase the applicable rate of interest by 5.00%, and exercise the other rights and remedies provided for under the Loan Agreements and related loan documents. The events of default under the Loan Agreements include payment defaults, breaches of covenants or representations and warranties, material adverse changes, certain bankruptcy events, cross defaults with certain other indebtedness, and judgment defaults.

Interest expense, including amortization of the debt discount, related to the Loan Agreements totaled $1.6 million for the year ended December 31, 2021. Accrued interest, included in accounts payable, was $0.1 million as of December 31, 2021. The outstanding Term Loan balance was $16.0 million as of December 31, 2021, inclusive of accretion of the final payment and net unamortized debt discount.

The estimated aggregate amounts and timing of payments on the Company's long-term debt obligations as of December 31, 2021 for the next five fiscal years are as follows:

2022	$ —
2023	3,657
2024	5,486
2025	5,486
2026	2,011
Subtotal	16,640
Unamortized discount	(643)
Total long-term debt, net	$ 15,997

PPP Loan

On April 10, 2020 the Company obtained an unsecured $1.1 million loan through JPMorgan Chase Bank, N.A. under the Paycheck Protection Program (the PPP Loan) pursuant to the Coronavirus Aid, Relief, and Economic Security Act (the CARES Act). The PPP Loan bore an interest rate of 0.98% and notionally matured two years from the date of issuance. Following the issuance of new, retroactive guidance on the program from the Small Business Administration on April 23, 2020, the Company repaid the PPP Loan principal and accrued interest in full. Interest expense related to the PPP Loan was de minimis for the year ended December 31, 2020.

7. Leases

Operating Leases

The Company has existing operating leases for certain office equipment and its facility with initial terms ranging from 36 months to 130 months. The facility lease has an option for the Company to extend the lease term for an additional five years; however, it is not reasonably certain the Company will exercise the option to renew when the lease term ends in 2027, and thus, the incremental term was excluded from the calculation of the lease liability and ROU asset. The Company has the right to terminate the lease at the end of the 94th month of the lease term if it is acquired by a third party and pays an early termination fee.

In July 2021, the Company entered into a lease for certain equipment with an initial term of 36 months, which includes a purchase option at the end of the lease term based upon the then fair market value of the equipment. The lease payment includes customary principal and interest as well as costs related to the installation and setup of the equipment. The Company evaluated the lease in accordance with ASC 842 and recorded this lease as an operating lease in the balance sheets. The ROU assets associated with all the Company's operating leases are recognized in the balance sheets.

Finance Leases

In November 2021, the Company entered into a lease for certain computer equipment with an initial term of 48 months, which includes an option to purchase the equipment at the end of the lease term that is not reasonably certain to be exercised. The lease payment includes customary principal and interest as well as costs related to the installation and setup of the equipment. The associated ROU asset is recognized within property and equipment, net in the balance sheets and is being amortized over four years in accordance with the Company's standard depreciation and amortization policies.

	Years Ended December 31,	
Lease expenses:	**2021**	**2020**
Operating lease expenses	$ 3,162	$ 3,137
Variable lease expenses	934	793
Total lease expenses	$ 4,096	$ 3,930

Lease Maturities:

	Operating Leases	Finance Leases	Total
2022	$ 3,365	$ 91	$ 3,456
2023	3,464	91	3,555
2024	3,554	91	3,645
2025	3,642	83	3,725
2026	3,751	—	3,751
Thereafter	2,891	—	2,891
Total minimum lease payments	20,667	356	21,023
Imputed interest	(5,111)	(57)	(5,168)
Total	15,556	299	15,855
Less: leases, current	(3,364)	(91)	(3,455)
Leases, net of current	$ 12,192	$ 208	$ 12,400

8. Fair Value

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

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

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

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

As of December 31, 2021 and 2020, the Company held no assets or liabilities measured at fair value on a nonrecurring basis and no liabilities measured at fair value on a recurring basis. The following fair value hierarchy table presents the Company's assets measured at fair value on a recurring basis (in thousands):

	Fair Value Measurement at Reporting Date Using			
	Total	Level 1	Level 2	Level 3
December 31, 2021:				
Assets				
Money market funds	$ 71,493	$ 71,493	$ —	$ —
	$ 71,493	$ 71,493	$ —	$ —
December 31, 2020:				
Assets				
Money market funds	$ 23,278	$ 23,278	$ —	$ —
U.S. Treasury securities	55,086	55,086	—	—
Certificates of deposit	490	—	490	—
	$ 78,854	$ 78,364	$ 490	$ —

9. Stockholders' Equity

Common Stock Reserved for Future Issuance

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

	December 31,	
	2021	2020
Common stock options issued and outstanding	11,707,568	9,842,744
Pre-funded warrants to purchase common stock	11,111,110	4,000,000
Common stock reserved and available for future grant under the 2014 Equity Incentive Plan	1,500,062	2,553,854
Common stock reserved for issuance under ESPP	2,914,710	2,301,704
Unvested restricted stock units	1,650,250	—
Total common stock reserved for future issuance	28,883,700	18,698,302

July 2020 Sale of Common Stock and Pre-funded Warrants

In July 2020, the Company sold 17,275,000 shares of its common stock at a public offering price of $3.25 per share and sold pre-funded warrants to purchase 4,000,000 shares of its common stock at a public offering price of $3.249 per pre-funded warrant. After deducting underwriting discounts and commissions and offering expenses, the Company received net proceeds from the offering of $64.2 million. The public offering price for the pre-funded warrants was equal to the public offering price of the common stock, less the $0.001 per share exercise price of each pre-funded warrant. Per their terms, the outstanding pre-funded warrants to purchase shares of common stock may not be exercised if certain holders' ownership of the Company's common stock would exceed 4.99% following such exercise. The pre-funded warrants are exercisable immediately and do not contain an expiration date. The pre-funded warrants include a cashless exercise provision in the event registered shares are not available, and do not include any mandatory redemption provisions. The pre-funded warrants are recorded as a component of stockholders' equity within additional paid-in capital. The pre-funded warrants are included in the computation of basic net loss per share as the exercise price is nominal and may be exercised at any time until the pre-funded warrants are exercised in full. During the year ended December 31, 2021, none of the July 2020 pre-funded warrants were exercised; as of December 31, 2021, all of the July 2020 pre-funded warrants remained issued and outstanding.

April 2021 Sale of Common Stock and Pre-funded Warrants

In April 2021, the Company sold 8,298,890 shares of its common stock at a public offering price of $2.25 per share and sold pre-funded warrants to purchase 7,111,110 shares of its common stock at a public offering price of $2.249 per pre-funded warrant. After deducting underwriting discounts and commissions and offering expenses, the

Company received net proceeds from the offering of $32.2 million. The public offering price for the pre-funded warrants was equal to the public offering price of the common stock, less the $0.001 per share exercise price of each pre-funded warrant. Per their terms, the outstanding pre-funded warrants to purchase shares of common stock may not be exercised if certain holders' ownership of the Company's common stock would exceed a specified threshold following such exercise. The pre-funded warrants are exercisable immediately and do not contain an expiration date. The pre-funded warrants include a cashless exercise provision in the event registered shares are not available, and do not include any mandatory redemption provisions. The pre-funded warrants are recorded as a component of stockholders' equity within additional paid-in capital. The pre-funded warrants are included in the computation of basic net loss per share as the exercise price is nominal and may be exercised at any time until the pre-funded warrants are exercised in full. During the year ended December 31, 2021, none of the April 2021 pre-funded warrants were exercised; as of December 31, 2021, all of the April 2021 pre-funded warrants remained issued and outstanding.

10. Stock-Based Compensation and Equity Plans

2014 Equity Incentive Plan

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

The 2014 Plan permits the grant of incentive stock options to the Company's employees and the grant of nonstatutory stock options, restricted stock, restricted stock units, stock appreciation rights, performance units and performance shares to the Company's employees, directors and consultants. The Company accounts for stock-based compensation expense related to stock options by estimating the fair value on the date of grant using the Black-Scholes-Merton option pricing model, while market price of the Company's common stock at the date of grant is used for restricted stock unit awards. Options granted under the 2014 Plan are generally scheduled to vest over four years, subject to continued service, and subject to certain acceleration of vesting provisions, expire no later than 10 years from the date of grant. Options granted under the 2014 Plan must have a per share exercise price equal to at least 100% of the fair market value of a share of the common stock as of the date of grant. Restricted stock units granted under the 2014 Plan are generally scheduled to vest over two to three years.

Under the evergreen provision of the 2014 Plan, the number of shares available for issuance under the 2014 Plan includes an annual increase on the first day of each fiscal year equal to the lesser of (i) 2,500,000 shares; (ii) 5% of the outstanding shares of common stock as of the last day of the immediately preceding fiscal year; or (iii) such other amount as the Company's board of directors may determine. Effective January 1, 2022, the number of shares available for future issuance was increased by 2,500,000 shares so that the total available for future issuance as of January 1, 2022 was 4,000,062 shares.

As of December 31, 2021, 1,500,062 shares of common stock were available for future grant under the 2014 Plan. The following table summarizes stock option activity for the year ended December 31, 2021 (in thousands except per share amounts and years):

	Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (In Years)	Aggregate Intrinsic Value
Outstanding as of December 31, 2020	9,843	$ 4.11		
Granted	2,965	$ 4.26		
Exercised	(3)	$ 2.11		
Forfeited	(1,097)	$ 4.10		
Outstanding as of December 31, 2021	11,708	$ 4.15	6.8	$ 460
Options vested and expected to vest as of December 31, 2021	11,708	$ 4.15	6.8	$ 460
Options exercisable as of December 31, 2021	6,994	$ 4.44	5.6	$ 348

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

	Years Ended December 31,		
	2021	2020	2019
Weighted-average grant-date fair value per share of options granted during the period	$ 3.32	$ 2.68	$ 1.64
Cash received from options exercised during the period	6	206	5
Intrinsic value of options exercised during the period	1	59	2

The following table summarizes restricted stock unit activity for the year ended December 31, 2021 (share amounts in thousands):

	Restricted Stock Units	Weighted-Average Grant-Date Fair Value
Unvested as of December 31, 2020	—	$ —
Granted	1,697	$ 2.16
Vested	—	$ —
Forfeited	(47)	$ 2.16
Unvested as of December 31, 2021	1,650	$ 2.16

2014 Employee Stock Purchase Plan

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

purchase periods. The Company accounts for stock-based compensation expense related to ESPP rights by estimating the fair value on the date of grant using the Black-Scholes-Merton option pricing model.

The number of shares available for issuance under the ESPP includes an annual increase on the first day of each fiscal year, equal to the lesser of (i) 800,000 shares; (ii) 1.5% of the outstanding shares of common stock as of the last day of the immediately preceding fiscal year; or (iii) such other amount as the Company's board of directors may determine. Effective January 1, 2022, the number of shares available for future issuance was increased by 800,000 shares so that the total available for future issuance as of January 1, 2022 was 3,714,710 shares.

As of December 31, 2021, the Company had issued 707,333 shares of common stock under the ESPP and had 2,914,710 shares available for future issuance.

Stock-Based Compensation Expense

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

	Years Ended December 31,		
	2021	2020	2019
Stock Options:			
Risk-free interest rate	0.8%	1.5%	2.5%
Expected dividend yield	0.0%	0.0%	0.0%
Expected volatility	99.2%	96.7%	98.1%
Expected term (in years)	6.0	6.1	6.1
Employee Stock Purchase Plan:			
Risk-free interest rate	0.1%	0.1%	2.0%
Expected dividend yield	0.0%	0.0%	0.0%
Expected volatility	90.9%	69.8%	69.5%
Expected term (in years)	1.3	1.3	1.3

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

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

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

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

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

	Years Ended December 31,		
	2021	2020	2019
Cost of product sales	$ 3	$ 13	$ 12
Research and development	3,355	2,456	2,085
Selling, general and administrative	4,039	3,642	2,793
Total stock-based compensation	$ 7,397	$ 6,111	$ 4,890

As of December 31, 2021, unrecognized compensation cost related to stock options was $11.1 million which is expected to be recognized over a remaining weighted-average vesting period of 2.5 years. As of December 31,

2021, unrecognized compensation cost related to restricted stock units was $2.8 million which is expected to be recognized over a remaining weighted-average vesting period of 2.2 years. As of December 31, 2021, unrecognized compensation cost related to ESPP rights was $0.2 million which is expected to be recognized over a remaining weighted-average vesting period of 1.3 years.

11. Collaboration Agreements

AGTC collaboration

In October 2019, the Company announced a strategic collaboration with AGTC to co-develop and co-commercialize an adeno-associated virus (AAV)-based gene therapy to restore hearing in patients with sensorineural hearing loss caused by a mutation in the GJB2 gene. Under the collaboration agreement, the Company and AGTC equally shared the program costs and any revenue or other proceeds related to the program through December 31, 2021. Effective January 1, 2022, the collaboration agreement was amended to increase the Company's responsibility for the overall development and commercialization of the program, which resulted in: (i) an increase in the Company's share of future product development costs and (ii) the Company's obligation to make potential future payments including royalties on any product sales in lieu of equal sharing of any profits or proceeds related to the program.

Co-Promotion Agreement

The Company entered into a co-promotion agreement with ALK-Abelló, Inc. (ALK) in June 2020, (the Co-Promotion Agreement) to support the promotion of OTIPRIO for the treatment of AOE in physician offices. During the term of the Co-Promotion Agreement, ALK reimbursed the Company for certain expenses, including a proportion of product support expenses; such payments were accounted for as reductions to selling, general and administrative expense. ALK was entitled to a share of gross profits totaling more than 50% from the sale of OTIPRIO to its accounts. The Company's payments to ALK for its portion of the gross profit were recognized as selling, general and administrative expense. The Company was the principal in the product sale of OTIPRIO and recognized all revenue and related cost of product sales. For the years ended December 31, 2021 and 2020, the Company recognized reductions in selling, general and administrative expenses related to the Co-Promotion Agreement of $0.5 million and $0.3 million, respectively. In May 2021, the Company sold the assets related to its OTIPRIO business to ALK.

12. Disposition of a Business

On May 28, 2021, the Company sold the assets related to OTIPRIO to ALK for an upfront payment of $0.8 million and additional potential amounts based on net sales of OTIPRIO for a specified period of time. The transaction was treated as a sale of a business. The contingent value of the remaining sale price will be measured and recognized in accordance with the gain contingency guidance which results in recognition when the gain is realized or realizable. The Company determined that the disposition of the business did not constitute a strategic shift and that it did not and will not have a major effect on its operations and financial results. Accordingly, the operations associated with the disposition are not reported in discontinued operations. The gain on sale of approximately $23,000 after accounting for liabilities transferred upon sale and the carrying amount of assets sold is recorded to selling, general and administrative expenses.

13. Income Taxes

Pursuant to Internal Revenue Code (IRC) Sections 382 and 383, annual use of the Company's net operating loss carryforwards may be subject to substantial annual limitations in the event a cumulative change in ownership of more than 50% occurs within a three-year period. If ownership changes within the meaning of IRC Section 382 are identified as having occurred, the amount of remaining tax attribute carryforwards available to offset future taxable income and income tax expense in future years may be significantly restricted or eliminated. Further, the Company's deferred tax assets associated with such tax attributes could be significantly reduced upon realization of an ownership change within the meaning of IRC Section 382. The Company completed an ownership change analysis pursuant to IRC Section 382 through December 31, 2020 and reduced deferred tax assets related to net operating loss carryforwards and research and development tax credit carryforwards accordingly. The Company is in the

process of completing an analysis through December 31, 2021 which could result in substantial limitations. When the analysis is completed, the Company will adjust deferred tax assets, if any, accordingly. Due to the existence of the full valuation allowance against the Company's net deferred tax assets, limitations created by ownership changes, if any, will not impact the Company's effective tax rate.

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

	December 31,	
	2021	2020
Deferred tax assets:		
Net operating loss carryforwards	$ 99,450	$ 88,013
Research and development credits	11,107	9,985
Depreciation and amortization	7,940	10,212
Accrued expenses	694	850
Lease liabilities	3,373	3,816
Stock compensation	4,083	3,856
Other, net	94	234
Total deferred tax assets	126,741	116,966
Less: valuation allowance	(124,040)	(113,826)
Total deferred tax assets, net of valuation allowance	2,701	3,140
Deferred tax liability:		
Right-of-use assets	(2,701)	(3,140)
Total deferred tax liability	(2,701)	(3,140)
Total	$ —	$ —

Due to the Company's history of losses and uncertainty regarding future earnings, a full valuation allowance has been recorded against the Company's net deferred tax assets, as it is more likely than not that such net assets will not be realized. A valuation allowance of approximately $124.0 million and $113.8 million has been established as of December 31, 2021 and 2020, respectively.

At December 31, 2021, the Company had federal and state net operating loss carryforwards of approximately $436.7 million and $127.1 million, respectively. Of the federal net operating loss carryforwards, approximately $196.1 million were generated in a taxable year beginning after December 31, 2017, and therefore do not expire. Federal net operating losses that occur after January 1, 2018 are subject to a taxable income limitation of 80% in accordance with the Tax Cuts and Jobs Act of 2017 (the Tax Act). The remaining federal and state net operating loss carryforwards will begin to expire in 2030, unless previously utilized. As of December 31, 2021, the Company also had federal and California research and development credit carryforwards of approximately $13.4 million and $6.5 million, respectively. The federal research and development credit carryforwards will begin expiring in 2030, unless previously utilized. The California research credit will carry forward indefinitely.

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

	2021	2020	2019
Federal statutory rate	$ (10,748)	$ (9,393)	$ (9,382)
State tax (net of federal benefit)	500	334	299
Permanent items, other	11	9	189
Stock compensation	1,349	1,595	2,470
Other adjustments	(204)	687	523
Research and development credits	(1,870)	(1,774)	(1,595)
Uncertain tax positions	748	710	638
Change in valuation allowance	10,214	7,832	6,858
Provision for income taxes	$ 0	$ 0	$ 0

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

	December 31,		
	2021	2020	2019
Balance at the beginning of the year	$ 11,514	$ 10,739	$ 10,052
Adjustments related to prior year tax positions	(83)	(21)	(80)
Increases related to current year tax positions	885	796	767
	$ 12,316	$ 11,514	$ 10,739

The Company's policy is to include interest and penalties related to unrecognized income tax benefits as a component of income tax expense. The Company has no accruals for interest or penalties in the balance sheets as of December 31, 2021 and 2020 and has not recognized interest or penalties in the statements of operations for the years ended December 31, 2021, 2020 and 2019.

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

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

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

None.

Item 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Management, with the participation of our Chief Executive Officer and our Chief Financial and Business Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2021. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2021, our Chief Executive Officer and our Chief Financial and Business Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act). Our management conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria established in "Internal Control—Integrated Framework" (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on the assessment, management has concluded that our internal control over financial reporting was effective as of December 31, 2021. This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm on our internal control over financial reporting due to our status as a non-accelerated filer.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the quarter ended December 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations of Disclosure Controls and Internal Control over Financial Reporting

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

Item 9B. OTHER INFORMATION

None.

Item 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

Item 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this item will be contained in our definitive proxy statement to be filed with the Securities and Exchange Commission in connection with our 2022 annual meeting of stockholders (Proxy Statement), which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2021, and is incorporated in this report by reference.

Item 11. EXECUTIVE COMPENSATION

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

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

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

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

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

Item 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

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

PART IV

Item 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

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

(1) Financial Statements:

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

(2) Financial Statement Schedules:

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

(3) Exhibits:

The following exhibits, as required by Item 601 of Regulation S-K are attached or incorporated by reference as stated below.

EXHIBIT INDEX

Exhibit Number	Description	Incorporation by Reference			
		Form	File No.	Exhibit	Filing Date
2.1#	Asset Transfer Agreement between the Registrant and IncuMed, LLC, dated April 30, 2013.	S-1	333-197365	2.1	7/11/2014
3.1	Amended and Restated Certificate of Incorporation of the Registrant.	S-1/A	333-197365	3.2	8/1/2014
3.2	Amended and Restated Bylaws of the Registrant.	8-K	001-36591	3.1	7/9/2020
4.1	Third Amended and Restated Investors' Rights Agreement among the Registrant and certain of its stockholders, dated April 23, 2014.	S-1	333-197365	4.1	7/11/2014
4.2	Specimen common stock certificate of the Registrant.	S-1/A	333-197365	4.2	7/28/2014
4.3	Description of securities registered pursuant to Section 12 of the Securities Exchange Act of 1934.	10-K	001-36591	4.3	2/27/2020
4.4	Form of Pre-Funded Warrant.	8-K	001-36591	4.1	7/10/2020
10.1+	Executive Employment Agreement between the Registrant and Paul E. Cayer.				
10.2+	Executive Employment Agreement between the Registrant and Robert Michael Savel, II.				
10.3+	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers.	S-1/A	333-197365	10.1	8/1/2014
10.4+	Amended and Restated 2010 Equity Incentive Plan and forms of agreement thereunder.	S-1/A	333-197365	10.2	8/1/2014
10.5+	2014 Equity Incentive Plan and forms of agreements thereunder.	S-1/A	333-197365	10.3	8/1/2014
10.6+	2014 Employee Stock Purchase Plan and form of agreement thereunder.	S-1/A	333-197365	10.4	8/1/2014
10.7+	Executive Incentive Compensation Plan.	S-1/A	333-197365	10.5	7/28/2014
10.8+	Executive Employment Agreement between the Registrant and David A. Weber, Ph.D.	S-1/A	333-197365	10.6	8/1/2014
10.9+	Executive Employment Agreement between the Registrant and Alan C. Foster, Ph.D.	10-Q	001-36591	10.2	8/4/2021
10.10#	License and Commercialization Agreement between the Registrant and DURECT Corporation, dated April 30, 2013.	S-1	333-197365	10.11	7/11/2014
10.11#	License Agreement between the Registrant and The Regents of the University of California, dated November 5, 2008, as amended on January 27, 2010, June 9, 2010 and November 7, 2012.	S-1	333-197365	10.12	7/11/2014
10.12	Lease Agreement between the Registrant and ARE-SD Region No. 34, LLC, dated May 11, 2015.	10-Q	001-36591	10.2	5/12/2015

10.13	Loan and Security Agreement among the Registrant, Oxford Finance LLC, as collateral agent, and the lenders party thereto from time to time, dated December 31, 2018.	8-K	001-36591	10.1	1/3/2019
10.14	Third Amendment to Loan and Security Agreement among the Company, Oxford Finance LLC, as collateral agent, and the lenders party thereto from time to time, dated June 2, 2021.	10-Q	001-36591	10.1	8/4/2021
10.15	Sales Agreement, dated as of August 4, 2021, between the Registrant and Cowen and Company, LLC.	8-K	001-36591	1.1	8/4/2021
23.1	Consent of Independent Registered Public Accounting Firm.				
24.1	Power of Attorney, incorporated by reference to the signature page hereto.				
31.1	Certification of Chief Executive Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
31.2	Certification of Chief Financial Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
32.1*	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				
32.2*	Certification of Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				
101.INS	Inline XBRL Instance Document.	The instance document does not appear in the interactive data file because its XBRL tags are embedded within the inline XBRL document.			
101.SCH	Inline XBRL Taxonomy Extension Schema Document.				
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.				
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.				
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.				
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.				
104	Cover page interactive data file (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibit 101).				

* The certifications attached as Exhibit 32.1 and 32.2 that accompany this Annual Report on Form 10-K are not deemed filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of Otonomy, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as

amended, whether made before or after the date of this Annual Report on Form 10-K, irrespective of any general incorporation language contained in such filing.
Portions of the exhibit have been omitted pursuant to an order granted by the Securities and Exchange Commission for confidential treatment.
+ Indicates management contract or compensatory plan.

Item 16. FORM 10-K SUMMARY

None.

SIGNATURES

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

Date: February 28, 2022

OTONOMY, INC.

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

POWER OF ATTORNEY

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

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

Signature	Title	Date
/s/ David A. Weber David A. Weber, Ph.D.	President, Chief Executive Officer and Director *(Principal Executive Officer)*	February 28, 2022
/s/ Paul E. Cayer Paul E. Cayer	Chief Financial and Business Officer *(Principal Financial and Accounting Officer)*	February 28, 2022
/s/ Jay Lichter Jay Lichter, Ph.D.	Chairman of the Board of Directors	February 28, 2022
/s/ James Breitmeyer James Breitmeyer, M.D., Ph.D.	Director	February 28, 2022
/s/ Jill M. Broadfoot Jill M. Broadfoot	Director	February 28, 2022
/s/ Vickie Capps Vickie Capps	Director	February 28, 2022
/s/ Ciara Kennedy Ciara Kennedy, Ph.D.	Director	February 28, 2022
/s/ Iain McGill Iain McGill	Director	February 28, 2022
/s/ Theodore R. Schroeder Theodore R. Schroeder	Director	February 28, 2022

Executive Team

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

Jeffery J. Anderson, Ph.D.
Vice President, Clinical Sciences

Breianna Bowen
Vice President, Human Resources

James Branch, CPA
Vice President, Finance and Controller

Paul E. Cayer
Chief Financial and Business Officer

Barbara M. Finn
Senior Vice President, Regulatory Affairs and Quality Assurance

Alan C. Foster, Ph.D.
Chief Scientific Officer

Erik Nelson
Vice President, Information Technology and Facilities

Fabrice Piu, Ph.D.
Senior Vice President, Preclinical Development

James Robinson
Vice President, Biometrics and Data Sciences

Robert M. Savel, II
Chief Technical Officer

David Skarinsky
Senior Vice President, Clinical

Anna Stepanenko
Vice President, Technical Operations

Board of Directors

Jay Lichter, Ph.D.
Chairman and Co-Founder

James B. Breitmeyer, M.D., Ph.D.
Board Member

Jill M. Broadfoot
Board Member

Vickie Capps
Board Member

Ciara Kennedy, Ph.D.
Board Member

Iain McGill
Board Member

Theodore R. Schroeder
Board Member

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

Corporate Headquarters
4796 Executive Drive
San Diego, CA 92121

Investor Information
Exchange: NASDAQ
Ticker symbol: OTIC
E-mail contact: ir@otonomy.com
Website: www.otonomy.com

Annual Meeting of Stockholders
June 21, 2022, 8:00 am PDT
Otonomy, Inc.
www.proxydocs.com/OTIC

Transfer Agent
EQ Shareowner Services
1110 Centre Pointe Curve, Suite 101 Mendota Heights, MN 55120
(800) 468-9716
www.equiniti.com

Independent Registered Public Accounting Firm
Ernst & Young LLP
San Diego, CA

Legal Counsel
Wilson Sonsini Goodrich & Rosati, P.C.
650 Page Mill Road
Palo Alto, CA 94304

Note on Forward-Looking Statements

This annual report contains forward-looking statements within the meaning of the U.S. securities laws. Such forward-looking statements are subject to risks and uncertainties that could cause Otonomy's actual results to differ materially from those indicated by these forward-looking statements. Information on the risks and uncertainties that could affect Otonomy's results is included in the Form 10-K included in this annual report. Otonomy undertakes no obligations to update any forward-looking statements.

Otonomy, Inc.
4796 Executive Drive
San Diego, CA 92121
www.otonomy.com