

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

FORM 10-Q

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

For the quarterly period ended March 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
(State or other jurisdiction of
incorporation or organization)

26-2590070
(I.R.S. Employer
Identification Number)

**4796 Executive Drive
San Diego, California 92121
(619) 323-2200**

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

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 Stock Market LLC (The NASDAQ Global Select Market)

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 is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes No

The number of shares of the registrant's common stock, par value \$0.001, outstanding as of May 6, 2021 was 56,618,092.

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PART I. FINANCIAL INFORMATION

Item 1. Financial Statements

Otonomy, Inc.

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

	March 31, 2021 (unaudited)	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	\$ 51,016	\$ 30,767
Short-term investments	22,813	55,576
Prepaid and other current assets	3,048	2,372
Total current assets	76,877	88,715
Restricted cash	702	702
Property and equipment, net	1,881	2,766
Right-of-use assets	13,724	14,082
Other long-term assets	222	—
Total assets	<u>\$ 93,406</u>	<u>\$ 106,265</u>
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	\$ 573	\$ 849
Accrued expenses	3,105	2,953
Accrued compensation	1,801	3,927
Long-term debt, current	1,957	—
Leases, current	3,260	3,265
Total current liabilities	10,696	10,994
Long-term debt, net of current	13,246	15,158
Leases, net of current	13,440	13,847
Total liabilities	37,382	39,999
Commitments and Contingencies		
Stockholders' equity:		
Preferred stock, \$0.001 par value; 10,000,000 shares authorized at March 31, 2021 and December 31, 2020; no shares issued or outstanding at March 31, 2021 and December 31, 2020	—	—
Common stock, \$0.001 par value; 200,000,000 shares authorized at March 31, 2021 and December 31, 2020; 48,319,202 and 48,318,970 shares issued and outstanding at March 31, 2021 and December 31, 2020, respectively	48	48
Additional paid-in capital	572,805	570,841
Accumulated other comprehensive income	5	1
Accumulated deficit	(516,834)	(504,624)
Total stockholders' equity	56,024	66,266
Total liabilities and stockholders' equity	<u>\$ 93,406</u>	<u>\$ 106,265</u>

See accompanying notes.

Otonomy, Inc.

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

	Three Months Ended March 31,	
	2021	2020
	(unaudited)	
Product sales, net	\$ 90	\$ 160
Costs and operating expenses:		
Cost of product sales	230	214
Research and development	7,660	7,672
Selling, general and administrative	4,043	3,836
Total costs and operating expenses	<u>11,933</u>	<u>11,722</u>
Loss from operations	(11,843)	(11,562)
Other income (expense)		
Interest income	15	193
Interest expense	(382)	(394)
Net loss	<u>\$ (12,210)</u>	<u>\$ (11,763)</u>
Net loss per share, basic and diluted	<u>\$ (0.23)</u>	<u>\$ (0.38)</u>
Weighted-average shares used to compute net loss per share, basic and diluted	<u>52,319,101</u>	<u>30,814,211</u>

See accompanying notes.

Otonomy, Inc.

Condensed Statements of Comprehensive Loss
(in thousands)

	<u>Three Months Ended March 31,</u>	
	<u>2021</u>	<u>2020</u>
	(unaudited)	
Net loss	\$ (12,210)	\$ (11,763)
Other comprehensive income:		
Unrealized gain on available for sale securities	4	53
Comprehensive loss	<u>\$ (12,206)</u>	<u>\$ (11,710)</u>

See accompanying notes.

Otonomy, Inc.

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

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2020	48,318,970	\$ 48	\$ 570,841	\$ 1	\$ (504,624)	\$ 66,266
Issuance of common stock upon exercise of stock options (unaudited)	232	—	1	—	—	1
Stock-based compensation expense (unaudited)	—	—	1,963	—	—	1,963
Net loss (unaudited)	—	—	—	—	(12,210)	(12,210)
Unrealized gain on available- for-sale securities (unaudited)	—	—	—	4	—	4
Balance at March 31, 2021 (unaudited)	<u>48,319,202</u>	<u>\$ 48</u>	<u>\$ 572,805</u>	<u>\$ 5</u>	<u>\$ (516,834)</u>	<u>\$ 56,024</u>
	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2019	30,814,211	\$ 31	\$ 500,084	\$ 11	\$ (459,893)	\$ 40,233
Stock-based compensation expense (unaudited)	—	—	1,414	—	—	1,414
Net loss (unaudited)	—	—	—	—	(11,763)	(11,763)
Unrealized gain on available- for-sale securities (unaudited)	—	—	—	53	—	53
Balance at March 31, 2020 (unaudited)	<u>30,814,211</u>	<u>\$ 31</u>	<u>\$ 501,498</u>	<u>\$ 64</u>	<u>\$ (471,656)</u>	<u>\$ 29,937</u>

See accompanying notes.

Otonomy, Inc.

Condensed Statements of Cash Flows
(in thousands)

	Three Months Ended March 31,	
	2021	2020
	(unaudited)	
Cash flows from operating activities:		
Net loss	\$ (12,210)	\$ (11,763)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	221	286
Stock-based compensation	1,963	1,414
Amortization of premiums (accretion of discounts) on short-term investments	22	(35)
Amortization of debt discount	45	50
Impairment of property, plant and equipment	727	—
Changes in operating assets and liabilities:		
Prepaid and other assets	(898)	281
Accounts payable	(209)	(264)
Accrued expenses	152	(917)
Accrued compensation	(2,126)	(1,164)
Right-of-use assets and lease liabilities, net	(54)	(29)
Net cash used in operating activities	<u>(12,367)</u>	<u>(12,141)</u>
Cash flows from investing activities:		
Purchases of short-term investments	—	(3,004)
Maturities of short-term investments	32,745	21,000
Purchases of property and equipment	(130)	(10)
Net cash provided by investing activities	<u>32,615</u>	<u>17,986</u>
Cash flows from financing activities:		
Proceeds from exercise of stock options	1	—
Net cash provided by financing activities	<u>1</u>	<u>—</u>
Net change in cash, cash equivalents and restricted cash	20,249	5,845
Cash, cash equivalents and restricted cash at beginning of period	31,469	25,895
Cash, cash equivalents and restricted cash at end of period	<u>\$ 51,718</u>	<u>\$ 31,740</u>
Cash and cash equivalents at end of period	\$ 51,016	\$ 31,038
Restricted cash at end of period	702	702
Cash, cash equivalents and restricted cash at end of period	<u>\$ 51,718</u>	<u>\$ 31,740</u>
Supplemental cash flow disclosures		
Cash paid for interest	<u>\$ 338</u>	<u>\$ 341</u>
Supplemental disclosure of non-cash investing activities:		
Purchase of property and equipment in accounts payable and accrued expenses	<u>\$ —</u>	<u>\$ 63</u>

See accompanying notes.

**Notes to Condensed Financial Statements
(unaudited)**

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 a Phase 2 trial for tinnitus; OTO-413, for which the Company is planning to initiate a Phase 1/2 expansion trial for hearing loss; and OTO-825, a gene therapy for congenital hearing loss, in IND-enabling activities. Additionally, the Company is conducting preclinical development for OTO-510 in otoprotection and OTO-6XX for severe hearing loss.

OTO-313 is a sustained-exposure formulation of the potent and selective N-Methyl-D-Aspartate (NMDA) receptor antagonist gacyclidine that demonstrated positive top-line results in a Phase 1/2 clinical trial in tinnitus patients. The Company has recently initiated a Phase 2 clinical trial for OTO-313 with top-line results expected in mid-2022. OTO-413 is a sustained-exposure formulation of brain-derived neurotrophic factor (BDNF) that demonstrated positive top-line results in a Phase 1/2 clinical trial in hearing loss patients. The Company plans to initiate an expansion of the Phase 1/2 clinical trial for OTO-413 in the second quarter of 2021 with top-line results expected in mid-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. Otonomy is conducting investigational new drug (IND)-enabling activities for OTO-825 in conjunction with Applied Genetic Technologies Corporation (AGTC), the Company's strategic collaborator for the program. In addition, Otonomy is conducting preclinical development for OTO-510, a novel molecule in development for the prevention of cisplatin-induced hearing loss, and OTO-6XX, a hair cell repair and regeneration program for severe hearing loss that includes a novel compound exclusively licensed to Otonomy from Kyorin Pharmaceutical Co., Ltd. (Kyorin).

Otonomy recently completed a third Phase 3 trial for OTIVIDEX, a sustained exposure formulation of the steroid dexamethasone, in Ménière's disease that failed to achieve its primary endpoint. Based on a comprehensive analysis of the results, the Company has decided to not pursue any further development of the product candidate. Following the negative OTIVIDEX trial results, the Company initiated a review of strategic alternatives for its commercial product, OTIPRIO. In 2020, the Company entered into a co-promotion agreement with ALK-Abelló, Inc. (ALK) to support the promotion of OTIPRIO for the treatment of AOE in physician offices in the United States and for use during ear tube placement surgery in pediatric patients.

Liquidity and Financial Condition

The Company follows Accounting Standards Codification (ASC) Topic 205-40, *Presentation of Financial Statements—Going Concern*, which requires that management evaluate whether there are relevant conditions and events that in aggregate raise substantial doubt about the entity'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.

The condensed 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 March 31, 2021, the Company had cash, cash equivalents and short-term investments of \$73.8 million, outstanding debt of \$15.2 million and an accumulated deficit of \$516.8 million. In April 2021, the Company sold in a public offering 8,298,890 shares of its common stock, which includes the underwriters' full exercise of their option to purchase additional shares, and the Company sold pre-funded warrants to purchase 7,111,110 shares of its common stock, for approximately \$32.1 million in total net proceeds after deducting underwriting discounts and commissions and estimated offering expenses. 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.

Basis of Presentation

The accompanying interim condensed financial statements are unaudited. These unaudited interim condensed financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (GAAP) and following the requirements of the United States Securities and Exchange Commission (SEC) for interim reporting. As permitted under those rules, certain footnotes or other financial information that are normally required by GAAP can be condensed or omitted. In the Company's opinion, the unaudited interim condensed financial statements have been prepared on the same basis as the audited financial statements and include all adjustments, which include only normal recurring adjustments necessary for the fair presentation of the Company's financial position, results of operations and cash flows for the periods presented. These condensed financial statements do not include all disclosures required by GAAP and should be read in conjunction with the Company's audited financial statements and accompanying notes for the year ended December 31, 2020 included in the Company's Annual Report on [Form 10-K](#), as filed with the SEC on February 11, 2021. The results presented in these unaudited condensed financial statements are not necessarily indicative of the results expected for the full fiscal year or any other interim period or any future year or period.

2. Summary of Significant Accounting Policies

Use of Estimates

The condensed financial statements have been prepared in accordance with 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.

Short-term Investments

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 both Level 1 and Level 2 financial instruments in the fair value hierarchy (see Note 6 – *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 condensed statements of comprehensive loss and as a separate component of stockholders' equity on the condensed 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.

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 able to enroll patients, among other activity. 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 generally adopting a work from home policy in line with directives from the State of California and the applicable local governments, and guidance from the U.S. Centers for Disease Control and Prevention (CDC). On-site activities have been restricted to certain essential facility and laboratory support functions and various safety protocols have been implemented.

Recent Accounting Pronouncements

Not Yet Adopted

In June 2016, Accounting Standards Update (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.

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 condensed 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 \$48.0 million and \$23.3 million as of March 31, 2021 and December 31, 2020, respectively. Available-for-sale debt securities with maturities of more than three months from the date of purchase have been classified as short-term investments, and were as follows (in thousands):

	Amortized Cost	Unrealized Gains	Unrealized Losses	Market Value
March 31, 2021:				
U.S. Treasury securities	\$ 22,563	\$ 5	\$ —	\$ 22,568
Certificates of deposit	245	—	—	245
	<u>\$ 22,808</u>	<u>\$ 5</u>	<u>\$ —</u>	<u>\$ 22,813</u>
December 31, 2020:				
U.S. Treasury securities	\$ 55,085	\$ 2	\$ (1)	\$ 55,086
Certificates of deposit	490	—	—	490
	<u>\$ 55,575</u>	<u>\$ 2</u>	<u>\$ (1)</u>	<u>\$ 55,576</u>

As of March 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 March 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

Prepaid and Other Current Assets

Prepaid and other current assets in the condensed balance sheets includes inventory, which is recorded at the lower of cost or net realizable value.

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

	March 31, 2021	December 31, 2020
Inventory	\$ 455	\$ 227
Other	2,593	2,145
Total	\$ 3,048	\$ 2,372

Property and Equipment, Net

Property and equipment is recorded at cost and depreciated over the estimated useful lives of the assets. Leasehold improvements are stated at cost and are depreciated over the lesser of the remaining term of the related lease or the estimated useful lives of the assets. The Company periodically assesses the value of its long-lived assets for impairment. During the three months ended March 31, 2021, the Company recorded an impairment to property and equipment, net of \$0.7 million. No impairment was recorded during the three months ended March 31, 2020.

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

	March 31, 2021	December 31, 2020
Laboratory equipment	\$ 4,272	\$ 4,265
Manufacturing equipment	348	1,075
Computer equipment and software	1,045	989
Leasehold improvements	768	768
Office furniture	1,548	1,548
	7,981	8,645
Less: accumulated depreciation	(6,100)	(5,879)
Total	\$ 1,881	\$ 2,766

Accrued Expenses

Accrued expenses are comprised of the following (in thousands):

	March 31, 2021	December 31, 2020
Accrued clinical trial costs	\$ 946	\$ 1,477
Accrued other	2,159	1,476
Total	\$ 3,105	\$ 2,953

5. Commitments and Contingencies

Intellectual Property Licenses

The Company has acquired exclusive rights to develop patented rights, information rights and related know-how for OTIPRIO, OTIVIDEX, OTO-311, OTO-313 and OTO-413 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 OTIPRIO, OTIVIDEX, OTO-313 and OTO-413 as follows (in thousands):

Development	\$ 1,250
Regulatory	10,275
Commercialization	1,000
Total	\$ 12,525

Under one of these agreements, the Company has achieved eight development milestones and one regulatory milestone, totaling \$3.2 million, related to its clinical trials for OTIPRIO, OTIVIDEX, OTO-311 and OTO-413.

In addition, the Company is obligated to pay royalties of less than five percent on net sales of OTIPRIO and on sales of any other commercial products developed using these licensed technologies. Such royalty expense for OTIPRIO is recorded to cost of product sales. The Company may also be obligated to pay to the licensors a percentage of fees received if and when the Company sublicenses the technology. As of March 31, 2021, the Company has not entered into any sublicense agreements for the licensed technologies.

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, with a payment of \$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.

Other Royalty Arrangements

The Company entered into an agreement related to OTIPRIO under which the Company is obligated to pay royalties of less than one percent on net product sales of OTIPRIO. The royalties are recorded as selling, general and administrative expense. The royalties are payable until the later of: (i) the expiration of the last to expire patent owned by the Company in such country covering OTIPRIO; or (ii) 10 years after the first commercial sale of OTIPRIO after receipt of regulatory approval for OTIPRIO in such country.

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.

6. Fair Value

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

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

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

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

As of March 31, 2021 and December 31, 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
March 31, 2021:				
Assets				
Money market funds	\$ 48,035	\$ 48,035	\$ —	\$ —
U.S. Treasury securities	22,568	22,568	—	—
Certificates of deposit	245	—	245	—
	<u>\$ 70,848</u>	<u>\$ 70,603</u>	<u>\$ 245</u>	<u>\$ —</u>
December 31, 2020:				
Assets				
Money market funds	\$ 23,278	\$ 23,278	\$ —	\$ —
U.S. Treasury securities	55,086	55,086	—	—
Certificates of deposit	490	—	490	—
	<u>\$ 78,854</u>	<u>\$ 78,364</u>	<u>\$ 490</u>	<u>\$ —</u>

7. Leases

The Company has existing operating leases for certain office equipment and its facility with initial terms ranging from 48 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. 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'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 the facility lease.

Lease expenses:	Three Months Ended March 31,	
	2021	2020
Operating lease expenses	\$ 785	\$ 784
Variable lease expenses	244	145
Total lease expenses	\$ 1,029	\$ 929

Lease Maturities:	Operating Leases	
Remaining in 2021	\$	2,429
2022		3,333
2023		3,433
2024		3,536
2025		3,642
2026		3,751
Thereafter		2,891
Total minimum lease payments		23,015
Imputed interest		(6,315)
Total		16,700
Less: leases, current		(3,260)
Leases, net of current	\$	13,440

8. Debt

Term Loan

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.

The Loan Agreement provides for a \$15.0 million secured term loan credit facility (the Term Loan). The proceeds of the Term Loan may be used for working capital and general corporate purposes. The Company has the right to prepay the Term Loan in whole or in part at any time, subject to a prepayment fee of 1.00%. Amounts prepaid or repaid under the Term Loan may not be reborrowed. The Term Loan was fully funded on the Closing Date and matures on December 1, 2023 (the Maturity Date). The Company paid a facility fee of 0.75% and customary closing fees on the Closing Date.

The Term Loan bears 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 March 31, 2021, the minimum interest rate). Interest on the Term Loan is payable monthly in arrears. The Company is permitted to make interest-only payments on the Term Loan for the 36 months following the Closing Date, followed by consecutive equal monthly payments of principal and interest in arrears through the Maturity Date. The outstanding principal amount of the Term Loan, together with accrued and unpaid interest, is due on December 1, 2023.

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

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

The Loan Agreement contains 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 Agreement contains 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 Loan is 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 Agreement 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 Agreement and related loan documents. The events of default under the Loan Agreement 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 Agreement totaled \$0.4 million for the three months ended March 31, 2021 and 2020. Accrued interest, included in accounts payable, was \$0.1 million as of March 31, 2021 and December 31, 2020. The outstanding Term Loan balance was \$15.2 million as of March 31, 2021 and December 31, 2020, inclusive of accretion of the final payment and net unamortized debt discount.

9. Stockholders' Equity

Common Stock Reserved for Future Issuance

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

	March 31, 2021	December 31, 2020
Common stock options issued and outstanding	11,893,024	9,842,744
Pre-funded warrants to purchase common stock	4,000,000	4,000,000
Common stock options available for future grant	3,014,710	2,553,854
Common stock reserved for issuance under ESPP	3,026,488	2,301,704
Total common stock reserved for future issuance	<u>21,934,222</u>	<u>18,698,302</u>

Net Loss Per Share

As of March 31, 2021 and 2020, potentially dilutive securities excluded from the calculation of diluted net loss per share consist of outstanding options to purchase 11,893,024 and 10,052,847 shares of the Company's common stock, respectively.

July 2020 Pre-funded Warrants

In July 2020, the Company sold pre-funded warrants to purchase 4,000,000 shares of its common stock with an exercise price of \$0.001 per pre-funded warrant, that do not contain an expiration date. During the three months ended March 31, 2021, none of the pre-funded warrants were exercised; as of March 31, 2021, all of the pre-funded warrants were issued and outstanding.

10. Stock-Based Compensation

The 2014 Equity Incentive Plan (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. 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. 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. Forfeitures are recognized as incurred. For awards subject to time-based vesting conditions, stock-based compensation expense is recognized using the straight-line method.

The following table summarizes stock option activity for the three months ended March 31, 2021 (share amounts in thousands):

	<u>Options</u>	<u>Weighted-Average Exercise Price</u>
Outstanding as of December 31, 2020	9,843	\$ 4.11
Granted	2,080	\$ 5.20
Exercised	(1)	\$ 3.17
Forfeited	(29)	\$ 4.25
Outstanding as of March 31, 2021	<u>11,893</u>	<u>\$ 4.30</u>

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

	<u>Three Months Ended March 31,</u>	
	<u>2021</u>	<u>2020</u>
Cost of product sales	\$ 3	\$ 5
Research and development	800	568
Selling, general and administrative	1,160	841
Total stock-based compensation	<u>\$ 1,963</u>	<u>\$ 1,414</u>

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 share the program costs and any revenue or other proceeds related to the program.

Co-Promotion Agreement

The Company entered into a co-promotion agreement with ALK in June 2020, (the Co-Promotion Agreement) to support the promotion of OTIPRIO for the treatment of AOE in physician offices. ALK reimburses the Company for certain expenses, including a proportion of product support expenses; such payments are accounted for as reductions to selling, general and administrative expense. ALK is 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 is recognized as selling, general and administrative expense. The Company is the principal in the product sale of OTIPRIO and recognizes all revenue and related cost of product sales. The Company recognized reductions in selling, general and administrative expenses related to the Co-Promotion Agreement of \$0.3 million for the three months ended March 31, 2021. Following the negative Phase 3 trial results for OTIVIDEX, the Company notified ALK of its intent to evaluate strategic alternatives for OTIPRIO.

12. Subsequent Event

Public Offering

In April 2021, the Company sold in a public offering 8,298,890 shares of its common stock, which includes the underwriters' full exercise of their option to purchase additional shares, and the Company sold pre-funded warrants to purchase 7,111,110 shares of its common stock, for approximately \$32.1 million in total net proceeds after deducting underwriting discounts and commissions and estimated offering expenses.

ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis of our financial condition and results of operations should be read together with our financial statements and the other financial information appearing elsewhere in this Quarterly Report on Form 10-Q. These statements generally relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. The following discussion and analysis contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Our actual results and the timing of events may differ materially from those discussed in our forward-looking statements as a result of various factors, including those discussed below and those discussed in the section titled "Risk Factors" included in this Quarterly Report on Form 10-Q.

Forward-looking statements may 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, including availability of top-line results from the ongoing Phase 2 clinical trial in tinnitus patients;
- our expectations regarding the clinical development of OTO-413, including availability of top-line results from the upcoming Phase 1/2 expansion clinical trial in hearing loss patients;
- our expectations regarding the future development of OTO-825 and our strategic collaboration with AGTC to develop and commercialize a gene therapy for congenital hearing loss;
- our expectations regarding the potential impacts on our business, preclinical programs and clinical trials due to the COVID-19 pandemic;
- the timing or likelihood of regulatory filings and approvals;
- our expectations regarding the future development of other product candidates, including but not limited to our development plans for our OTO-510 and OTO-6XX programs;
- our expectations regarding the evaluation of strategic alternatives for OTIPRIO;
- 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 loan 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 OTIPRIO and our product candidates; our ability to protect our intellectual property related to OTIPRIO and our product candidates in the United States and throughout the world; expectations regarding potential market size, opportunity and growth; our ability to manage operating expenses; implementation of our business model and strategic plans for our business, product candidates and technology; the risk of the occurrence of any event, change or other circumstance that could give rise to the termination of promotional or collaboration agreements; the risks of the occurrence of any event, change or other circumstances that could impact our ability to repay or comply with the terms of the loan provided by Oxford Finance LLC; and other risks. These forward-looking statements reflect our beliefs and views with respect to future events and are based on estimates and assumptions as of the date of this Quarterly Report on Form 10-Q 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 II, 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 Quarterly Report on Form 10-Q 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, OTIPRIO, 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 Quarterly Report on Form 10-Q to conform these statements to actual results or to changes in our expectations, except as required by law.

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

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 a Phase 2 trial for tinnitus; OTO-413, for which we are planning to initiate a Phase 1/2 expansion trial 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 for OTO-510 in 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 recently initiated a Phase 2 clinical trial for OTO-313, with top-line results expected in mid-2022.

OTO-413 is a sustained-exposure formulation of BDNF in development for the repair of cochlear synaptopathy, an underlying pathology in age-related and noise-induced hearing loss. In December 2020, we announced positive top-line results from a Phase 1/2 clinical trial of OTO-413, demonstrating that a single intratympanic injection of OTO-413 was well-tolerated and showed therapeutic activity across multiple speech-in-noise hearing tests. We plan to initiate an expansion of the Phase 1/2 trial in the second quarter of 2021 to evaluate a refined study protocol in additional hearing loss patients, with top-line results expected in mid-2022.

OTO-825 is a gene therapy targeting mutations in the GJB2 gene, which is the most common cause of congenital hearing loss. In October 2019, Otonomy and AGTC announced a collaboration to develop an adeno-associated virus (AAV) based gene therapy for patients with hearing loss caused by the GJB2 mutation. Based on preclinical studies, we have selected OTO-825 as a clinical candidate and are initiating activities required for an IND filing. We plan to provide an update on this program in mid-2021.

OTO-510 is a product candidate in preclinical development for the prevention of cisplatin-induced hearing loss (CIHL), which routinely occurs in patients undergoing chemotherapy with platinum-based agents. OTO-510 has demonstrated improved otoprotection in preclinical CIHL studies compared to other agents in 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.

The OTO-6XX program is focused on hair cell repair and regeneration for the treatment of severe hearing loss. In July 2020, we entered into a license agreement with Kyorin that provides us with exclusive worldwide rights to develop, manufacture and commercialize a novel compound from Kyorin that has demonstrated the ability to induce hair cell regeneration in a nonclinical proof-of-concept model. We are continuing to evaluate the potential of this compound for our OTO-6XX program.

OTIVIDEX is a product candidate for the treatment of Ménière's disease for which we completed three Phase 3 clinical trials. The AVERTS-1 trial failed its primary endpoint (p value = 0.62), while the parallel AVERTS-2 trial was successful (p value = 0.029). In order to support the filing of a New Drug Application to the FDA, we conducted a third trial with results announced in February 2021. This trial failed to achieve its primary endpoint, which is based on the intent-to-treat population (p value = 0.312). The trial did achieve statistical significance for the per protocol population (p value = 0.031). Based on a comprehensive analysis of the results, we have decided to not pursue additional development of OTIVIDEX.

In addition, we developed, received FDA approval for and commercially launched OTIPRIO (ciprofloxacin otic suspension) for use during tympanostomy tube placement (TTP) surgery in pediatric patients. OTIPRIO was also approved by the FDA for the treatment of acute otitis externa (AOE). In June 2020, we entered into a co-promotion agreement with ALK to support the promotion of OTIPRIO for the treatment of AOE in physician offices in the United States, which was amended in October 2020 to include promotion of OTIPRIO for use during TTP surgery in pediatric patients. Following the negative Phase 3 trial results for OTIVIDEX, we notified ALK of our intent to evaluate strategic alternatives for the product.

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. As of March 31, 2021, we had cash, cash equivalents and short-term investments of \$73.8 million and an outstanding debt balance of \$15.2 million.

We have never been profitable, and as of March 31, 2021, we had an accumulated deficit of \$516.8 million. Our net losses were \$12.2 million and \$11.8 million for the three months ended March 31, 2021 and 2020, 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.

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 approximately \$32.1 million in total net proceeds after deducting underwriting discounts and commissions and estimated offering 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;
- conduct preclinical development of OTO-825, 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 report. 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 able to enroll patients, among other activity. Nonetheless, we do not know the full extent of potential future delays or impacts on our business operations, our preclinical programs and clinical trials, healthcare systems, our financial condition, or the global economy as a whole resulting from the COVID-19 pandemic.

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

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;
- 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):

	Three Months Ended March 31,	
	2021	2020
Third-party development costs:		
OTIVIDEX	\$ 309	\$ 1,606
OTO-313	1,353	608
OTO-413	214	716
Total third-party development costs	1,876	2,930
Other unallocated internal research and development costs	5,784	4,742
Total research and development costs	\$ 7,660	\$ 7,672

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 management's discussion and analysis of our financial condition and results of operations is based on our condensed financial statements. 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.

We believe the estimates, assumptions and judgments involved in the accounting policies described in the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" in Item 7 of our Annual Report on [Form 10-K](#) for the year ended December 31, 2020, as filed with the SEC on February 11, 2021, have the greatest potential impact on our financial statements, so we consider them to be our critical accounting policies and estimates.

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 three months ended March 31, 2021 and 2020, 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 options granted to employees and directors, we recognize the resulting fair value as expense on a straight-line basis over the vesting period of each respective stock option, generally four years.

Results of Operations

Comparison of the Three Months Ended March 31, 2021 and 2020

The following table sets forth the significant components of our results of operations for the periods presented (in thousands):

	Three Months Ended March 31,		Change
	2021	2020	
Research and development	\$ 7,660	\$ 7,672	\$ (12)
Selling, general and administrative	4,043	3,836	207

Research and development expenses. Research and development expenses were consistent year-over-year due to a number of activities including: (i) a decrease of \$1.3 million in OTIVIDEX clinical trial and development costs primarily due to lower activity during 2021 as a result of the completion of the Phase 3 clinical trial; (ii) a decrease of \$0.5 million in development costs for our OTO-413 hearing loss program due to the completion of the initial dose cohorts of the clinical trial in 2020; offset by (iii) a \$0.8 million net increase in OTO-313 clinical trial and development costs; (iv) an increase of \$0.4 million in personnel costs; and (v) a \$0.6 million increase in facilities and other operating expenses mainly due to the impairment of OTIVIDEX manufacturing equipment.

Selling, general and administrative expenses. The increase of \$0.2 million in selling, general and administrative expenses was primarily related to an increase in other operating expenses.

Liquidity and Capital Resources

We have incurred significant losses and negative cash flows from operations since our inception. As of March 31, 2021, we had an accumulated deficit of \$516.8 million and we expect to continue to incur significant losses for the foreseeable future. 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.

As of March 31, 2021, we had cash, cash equivalents and short-term investments of \$73.8 million and an outstanding debt balance of \$15.2 million. 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.

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

	2021	2020
Net cash (used in) provided by:		
Operating activities	\$ (12,367)	\$ (12,141)
Investing activities	32,615	17,986
Financing activities	1	—
Net increase in cash, cash equivalents and restricted cash	<u>\$ 20,249</u>	<u>\$ 5,845</u>

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 \$12.4 million during the three months ended March 31, 2021 compared to \$12.1 million, for the prior year period. The \$0.3 million increase in the utilization of cash was primarily due to an increase in operating losses compared to the prior year period.

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 \$32.6 million during the three months ended March 31, 2021 compared to net cash provided by investing activities of \$18.0 million during the prior year period. The increase in net cash provided by investing activities was primarily due to net maturities 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.

April 2021 Financing

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 approximately \$32.1 million in total net proceeds after deducting underwriting discounts and commissions and estimated offering expenses.

At the Market Offering Program

In August 2019, we entered into a sales agreement (Sales Agreement) with Cowen and Company, LLC (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. Through March 31, 2021, we have not sold any shares under the Sales Agreement.

Term Loan

Oxford Loan

On December 31, 2018 (the Closing Date), we entered into a Loan and Security Agreement with Oxford Finance LLC (the Loan Agreement). The Loan Agreement provides for a \$15.0 million secured term loan credit facility (the Term Loan). The proceeds of the Term Loan may be used for working capital and general corporate purposes. We have the right to prepay the Term Loan in whole or in part at any time, subject to a prepayment fee of 1.00%. Amounts prepaid or repaid under the Term Loan may not be reborrowed. The Term Loan was fully funded on the Closing Date and matures on December 1, 2023 (the Maturity Date). We paid a facility fee of 0.75% and customary closing fees on the Closing Date.

The Term Loan bears 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 March 31, 2021, the minimum interest rate). Interest on the Term Loan is payable monthly in arrears. The Company is permitted to make interest-only payments on the Term Loan for the 36 months following the Closing Date, followed by consecutive equal monthly payments of principal and interest in arrears through the Maturity Date. The outstanding principal amount of the Term Loan, together with accrued and unpaid interest, is due on December 1, 2023. The net outstanding Term Loan balance was \$15.2 million as of March 31, 2021.

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

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

The Loan Agreement contains 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 Agreement contains customary negative covenants limiting our ability to, among other things, sell assets, allow a change of control to occur (if the Term Loan is 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 Agreement 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 Agreement and related loan documents. The events of default under the Loan Agreement 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 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 report. 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. 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 OTIPRIO and our product candidates, if approved;
- the costs related to manufacturing commercial supplies of OTIPRIO;
- 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.

Off-Balance Sheet Arrangements

During the periods presented we did not have, nor do we currently have, any off-balance sheet arrangements as defined under the applicable rules of the SEC.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

As a “smaller reporting company” as defined in Rule 12b-2 of the Securities Exchange Act of 1934, as amended (the Exchange Act), we are not required to provide the information required by this item.

ITEM 4. 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 March 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 March 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.

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 March 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.

PART II. OTHER INFORMATION

ITEM 1. 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 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 Quarterly Report on Form 10-Q, 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.
- OTIPRIO and 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.
- 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 other than OTIPRIO. The denial or delay of any such approval would delay commercialization and have a material adverse effect on our potential to generate revenue, our business and our results of operations.
- 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.
- OTIPRIO and our product candidates, if approved, will face significant competition in the biopharmaceutical industry, and our failure to effectively compete with competitor drugs, including off-label drug use, and future competitors may prevent us from achieving significant market penetration and expansion.
- 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 have not yet generated significant revenue, and we have decided not to pursue any further development of our product candidate OTIVIDEX following a recently completed 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, for which we are planning to initiate a Phase 1/2 expansion trial 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 \$12.2 million and \$11.8 million for the three months ended March 31, 2021 and 2020, respectively. As of March 31, 2021, we had an accumulated deficit of \$516.8 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 yet generated significant product revenue and may never become profitable.

We expect to continue to incur significant losses for the foreseeable future. Our ability to achieve significant revenue and profitability is dependent on our ability to complete the development of our product candidates, obtain necessary regulatory approvals and successfully commercialize our 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 have not generated significant revenue from sales of OTIPRIO. In June 2020, we entered into a co-promotion agreement with ALK to support the promotion of OTIPRIO for the treatment of AOE in physician offices in the United States, which was amended in October 2020 to include promotion of OTIPRIO for use during TTP surgery in pediatric patients. Following the negative Phase 3 trial results for OTIVIDEX, we notified ALK of our intent to evaluate strategic alternatives for the product.

We currently have limited 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 March 31, 2021, we had cash, cash equivalents and short-term investments of \$73.8 million and an outstanding debt balance of \$15.2 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 OTIPRIO and our product candidates, if approved;
- the revenue generated by OTIPRIO and our product candidates, if approved;
- the cost of commercialization activities for OTIPRIO and any of our product candidates that may be approved for sale, if any, including marketing, sales and distribution costs;
- the number and characteristics of any other product candidates we develop or acquire;
- our ability to establish and maintain strategic collaborations, licensing, development or commercialization arrangements and the terms and timing of such arrangements;
- the degree and rate of market acceptance of OTIPRIO and any other approved products;
- the emergence, approval, availability, perceived advantages, relative cost, relative safety and relative efficacy of other products or treatments;
- the expenses needed to attract and retain skilled personnel;
- the costs associated with being a public company;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims and other intellectual property rights, including litigation costs and the outcome of such litigation;
- the 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 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 March 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 commercialize our product, develop and commercialize our product candidates or operate as a business. Any collaboration agreements we enter into may provide capital in the near-term but limit our potential cash flow and revenue in the future. Any of the foregoing could significantly harm our business, financial condition and prospects.

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

Outbreaks of epidemic, pandemic or contagious diseases, such as COVID-19, could significantly disrupt our business. Such outbreaks pose the risk that we or our employees, contractors, suppliers, and other partners may be prevented from conducting business activities for an indefinite period of time due to spread of the disease, or due to shutdowns that may be requested or mandated by federal, state and local governmental authorities. Business disruptions could include disruptions or restrictions on our ability to travel, as well as temporary closures of our facility, the facilities of our partners, clinical trial sites, service providers, suppliers or contract manufacturers. While it is not possible at this time to estimate the overall impact that the COVID-19 pandemic could have on our business, the continued rapid spread of COVID-19, both across the United States and through much of the world, and the measures taken by the governments of countries and local authorities affected has disrupted and could delay our ongoing clinical trials, and could disrupt and delay our preclinical activities, the manufacture or shipment of both drug substance and finished drug product for preclinical testing and clinical trials and adversely impact our business, financial condition or operating results.

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

We have clinical trial sites in the United States and Europe, which may be affected by travel or quarantine restrictions imposed by federal, state or local governments due to the COVID-19 pandemic. 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 have made and we (and our CROs) may need to make certain adjustments to the operation of clinical trials in an effort to ensure the monitoring and safety of patients and minimize risks to trial data integrity during the pandemic in accordance with the guidance issued by the FDA 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) 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. Further, in June 2020, the FDA issued a guidance on good manufacturing practice considerations for responding to COVID-19 infection in employees in drug products manufacturing, including recommendations for manufacturing controls to prevent contamination of drugs. Such guidance and any future guidance or regulatory requirements impacting drug product manufacturing, including delays associated with complying with new requirements, could impact the operations of our contract manufacturers, our business, and our ability to obtain sufficient supplies for our clinical development on a timely basis.

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.

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; a list of all subjects affected by the COVID-19-pandemic related study disruption by unique subject identifier and by investigational site and a description of how the individual's participation was altered; and analyses and corresponding discussions that address the impact of implemented contingency measures (e.g., participant discontinuation from investigational product and/or study, alternative procedures used to collect critical safety and/or efficacy data) on the safety and efficacy results reported for the clinical trial.

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 have not yet generated 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, for which we are planning to initiate a Phase 1/2 expansion trial 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

OTIPRIO and 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.

OTIPRIO and our product candidates, if approved, may not achieve market acceptance among physicians and patients, and may not be commercially successful. For OTIPRIO, treatment of pediatric patients with bilateral otitis media with effusion undergoing TTP surgery is currently addressed with the off-label use of antibiotic ear drops, but antibiotic ear drops are approved for the AOE indication. We launched OTIPRIO in March 2016, but we have not generated significant revenue from sales of OTIPRIO. Since then, we have 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 AOE in physician offices in the United States, which was amended in October 2020 to include promotion of OTIPRIO for use during TTP surgery in pediatric patients. Following the negative Phase 3 trial results for OTIVIDEX, we notified ALK of our intent to evaluate strategic alternatives for the product.

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 OTIPRIO and our product candidates, if approved, will depend significantly on the adoption and use of the resulting products by physicians for approved indications. The decision to elect treatment with OTIPRIO for middle ear effusion in pediatric patients requiring TTP surgery and AOE, or to elect to utilize 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.

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 recently reported third Phase 3 clinical trial did not. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier clinical trials, and we cannot be certain that we will not face similar setbacks. Even if our clinical trials are completed, the results may not be sufficient to obtain regulatory approval for our product candidates or support the indications which we are pursuing.

From time to time, we may publicly disclose preliminary, interim or top-line data from our clinical trials. These interim updates are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously 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 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 other than OTIPRIO. The denial or delay of any such approval would delay commercialization and have a material adverse effect on our potential to generate revenue, our business and our results of operations.

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

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

- our inability to satisfactorily demonstrate that the product candidates are safe and effective for the requested indication;
- the FDA's disagreement with our trial protocol or the interpretation and analysis of data from nonclinical studies or clinical trials;
- the population studied in the clinical trial may not be sufficiently broad or representative to assess safety in the full population for which we seek approval;
- our inability to demonstrate that clinical or other benefits of our product candidates outweigh any safety or other perceived risks;
- the FDA's determination that additional nonclinical or clinical trials are required;
- the FDA's non-approval of the formulation, labeling or the specifications of our product candidates;
- the FDA's failure to accept the manufacturing processes or facilities of third-party manufacturers with which we contract, or our inability to manufacture our product candidates pursuant to cGMP; or
- the potential for approval policies or regulations of the FDA to significantly change in a manner rendering our clinical data insufficient for approval.

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

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

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

Some patients in our clinical trials have reported adverse events after being treated with OTIPRIO, OTIVIDEX, 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 or product candidates, the FDA and other foreign regulatory agency regulations will require that we promptly report certain information about adverse medical events if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We may fail to report adverse events we become aware of within the prescribed timeframe. We may also fail to appreciate that we have become aware of a reportable adverse event, especially if it is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of our product or product candidates. If we fail to comply with our reporting obligations, the FDA or other foreign regulatory agencies could take action including criminal prosecution, the imposition of civil monetary penalties, seizure of our products, or delay in approval or clearance of future products.

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

The biopharmaceutical industry is intensely competitive and subject to rapid and significant technological change. If approved, our products must compete with off-label drug use by physicians to treat the indications for which we seek approval, such as, in the case of OTIPRIO, the current use of inexpensive generic antibiotic ear drops to treat middle ear effusion in patients requiring TTP surgery. We are also aware that other companies, such as Akouos, Inc., Arbor Pharmaceuticals, LLC, Audion Therapeutics, Auris Medical Holding AG, Autifony Therapeutics Ltd., BridgeBio Pharma, Inc., Decibel Therapeutics, Inc., Fennec Pharmaceuticals Inc., Frequency Therapeutics, Laboratorios SALVAT S.A., Novartis AG, Otologic Pharmaceuticals Inc., Pipeline Therapeutics, Sensorion SA, Sound Pharmaceuticals Inc., Spiral Therapeutics, and Strekin AG are commercializing products or developing potential products for the treatment of various otic indications, including ear infections, 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 OTIPRIO and our product candidates.

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

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

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

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

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

We depend on the availability of key raw materials, including poloxamer for OTIPRIO and our product candidates, ciprofloxacin for OTIPRIO, gacyclidine for OTO-313, 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 and product candidates, we may need to engage alternate suppliers to prevent a possible disruption of the manufacture of the materials necessary to produce OTIPRIO for required commercial supplies or our product candidates for our clinical trials. We do not have any control over the availability of raw materials. If we or our manufacturers are unable to purchase these raw materials on acceptable terms, at sufficient quality levels, or in adequate quantities, if at all, commercial sales of OTIPRIO and the development of 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 for our product candidates or generate revenues from the sale of any approved products.

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

OTIPRIO is currently approved for the treatment of pediatric patients with bilateral otitis media with effusion undergoing TTP surgery and for the treatment of AOE. 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 or product candidates in the future, but we cannot predict when or if we will receive the regulatory approvals required to promote our product or product candidates for new treatment indications. Failure to receive such approvals prevents us from promoting and commercializing the new treatment indications. In addition, we would be required to conduct additional clinical trials or studies to support approvals for additional indications, which would be time consuming and expensive, and may produce results that do not support regulatory approvals. If we do not obtain additional regulatory approvals, our ability to expand our business will be limited.

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

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

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

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

We have limited experience in the marketing and sale of pharmaceutical products, and there are significant risks involved in managing a sales and marketing organization, including our ability to hire, retain, adequately compensate and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel and effectively manage a geographically dispersed sales and marketing team. For example, we discontinued promotional support for OTIPRIO and, as a result, no longer have a sales force. If we decide not to promote our product candidates ourselves, if approved, we may consider promotional partnership arrangements. For instance, in June 2020, we entered into a co-promotion agreement with ALK to support the promotion of OTIPRIO for the treatment of AOE in physician offices in the United States, which was amended in October 2020 to include promotion of OTIPRIO for use during TTP surgery in pediatric patients. Following the negative Phase 3 trial results for OTIVIDEX, we notified ALK of our intent to evaluate strategic alternatives for the product.

There are no assurances that such partnership for OTIPRIO, or 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 and product candidates, if approved, we may need to expand our development, regulatory, quality, managerial, sales and marketing, operational, finance and other resources to manage our operations and clinical trials, continue our development activities and commercialize our product candidates, if approved. If our operations expand, we expect that we will need to manage additional relationships with various manufacturers and collaborative partners, suppliers and other organizations.

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

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

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

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

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

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

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

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

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

In March 2010, the Affordable Care Act (ACA) became law in the United States. One goal of ACA is to reduce the cost of healthcare and substantially change the way healthcare is financed by both governmental and private insurers. While we cannot fully predict what impact on federal reimbursement policies this legislation will continue to have in general or on our business specifically, ACA may result in downward pressure on pharmaceutical reimbursement, which could negatively affect our ability to generate revenue, achieve market acceptance of our product or future approved products, attain profitability, or commercialize our product or any future approved products. Provisions of ACA relevant to the pharmaceutical industry include the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, not including orphan drug sales;
- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% (increased pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) point-of-sale discounts on negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report annually certain financial arrangements with physicians and teaching hospitals, as defined in the ACA and its implementing regulations, including reporting any payment or "transfer of value" provided to physicians, as defined by such law, and teaching hospitals and any ownership and investment interests held by physicians and their immediate family members during the preceding calendar year (effective January 1, 2022, these reporting obligations will extend to include payments and transfers of value made during the previous year to certain non-physician providers such as physician assistants and nurse practitioners);
- expansion of healthcare fraud and abuse laws, including the federal False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research.

There have been judicial and Congressional challenges to certain aspects of the ACA. 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. It is unclear how such litigation, 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. Until the ACA or other healthcare reform measures are fully implemented or there is more certainty concerning the future of the ACA or such healthcare reform measures, it will be difficult to predict its full impact and influence on our business.

Recently, the Trump administration announced four executive orders to lower drug prices, including allowing importation of certain drugs, changing how drug rebates are negotiated by middlemen, like pharmacy benefit managers, and directing such rebates to be passed to patients as point-of-sale discounts, and requiring Medicare to pay for certain Part B drugs at the lowest price available in economically comparable countries. In 2020, the Trump administration announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. In September 2020, FDA also issued a final guidance on importation of certain FDA-approved human prescription drugs and a final rule that sets forth requirements for an importation program for certain prescription drugs from Canada, allowing States, Indian Tribes, and, in certain circumstances, pharmacists and wholesalers, to submit proposals for importation for the FDA for review and authorization. In November 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturer. In December 2020, CMS issued a final rule implementing significant manufacturer price reporting changes 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. It is unclear how these new regulations and healthcare measures of the Biden administration will impact on our business. Healthcare reform measures that may be adopted in the future may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for our product or future approved products. Any such reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, achieve market acceptance of our product or future approved products, attain profitability, or commercialize future approved products.

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

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

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

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

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

Our success depends, in part, on our continued ability to attract, retain and motivate highly qualified management, commercial, clinical and scientific personnel. We believe that our future success is highly dependent upon the contributions of our senior management, particularly our President and Chief Executive Officer, as well as our senior scientists and other members of our senior management team. The loss of services of any of these individuals, who all have at-will employment arrangements with us, could delay or prevent the successful development of our product pipeline, completion of our planned clinical trials or the commercialization of our product candidates, if approved.

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

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

Although a substantial amount of our efforts are focused on the development and regulatory approval of our current product candidates, a key element of our strategy is to identify, develop and commercialize additional product candidates for the treatment of neurology disorders. We are seeking to do so through our internal research programs and may explore strategic collaborations with third parties for the development or acquisition of new product candidates or products. Research programs to identify new product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified or successfully developed.

Our internal computer systems, or those of our CROs or other contractors or consultants, or our partners, may fail or suffer security breaches, which could result in a material disruption of our drug development programs.

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

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

Generally accepted accounting principles in the United States are subject to interpretation by the Financial Accounting Standards Board, the SEC and various bodies formed to promulgate and interpret appropriate accounting principles. A change in accounting standards or practices can have a significant effect on our reported results and may even affect our reporting of transactions completed before the change is effective. New accounting pronouncements and varying interpretations of accounting pronouncements have occurred and may occur in the future. 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.

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

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

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

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

- economic weakness, including inflation, or political instability in non-U.S. economies and markets;
- differing and changing regulatory or legal requirements in non-U.S. countries;
- challenges enforcing our contractual and intellectual property rights, especially in non-U.S. countries that may not respect and protect intellectual property rights to the same extent as the United States;
- difficulties in compliance with non-U.S. laws and regulations;
- changes in non-U.S. 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.

Risks Related to Our Intellectual Property

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

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

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

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

Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after its effective filing date. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Without patent protection for our product or product candidates, we may be open to competition from generic versions of our product or product candidates. Further, if we encounter delays in our development efforts, including our clinical trials, the period of time during which we could market our product or product candidates under patent protection would be reduced.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

compelled to grant a license to our patents to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license. Finally, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws.

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

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

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

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

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

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

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

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

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

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

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, during the course of litigation or administrative proceedings, there could be public announcements of the results of hearings, motions or other interim proceedings or developments or public access to related documents. If investors perceive these results to be negative, the market price for our common stock could be significantly harmed.

Although not involving issued U.S. patents covering our product or any of our product candidates, on April 17, 2015, we filed a request for interference between one of our U.S. pending applications and a U.S. pending application controlled by Auris Medical Holding AG (Auris). On July 20, 2015, we received notice from the USPTO that the Patent Trial and Appeal Board (PTAB) declared an interference between our pending application and the Auris patent (issued as U.S. Patent No. 9,066,865 on June 30, 2015). On January 26, 2017, the PTAB determined that all of the Otonomy patent claims and all but one of the Auris patent claims were not patentable. We filed a Notice of Appeal on March 27, 2017, in which we asked the Federal Circuit to reverse PTAB's decision that our claims are not patentable and that Auris's single claim is. On August 1, 2018, the Federal Circuit agreed with us that the PTAB had erred in its rulings for Auris. The court reversed the PTAB's decision against Otonomy and remanded the case for the PTAB to enter judgment for Otonomy. On March 11, 2019, the PTAB entered the judgment for Otonomy and cancelled the Auris patent. On April 24, 2020, the USPTO issued a Notice of Allowance for our pending application, indicating that all of our claims are allowed. On September 15, 2020, the pending application was issued as U.S. Patent No. 10,772,828.

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

We are a party to a number of license agreements under which we are granted intellectual property rights that are crucial to our business. A portion of our patent portfolio for our product and certain product candidates was co-developed and is co-owned with UC which licensed its rights to us through an exclusive worldwide license agreement. Under our existing license agreement with UC, we are subject to various obligations, including development and commercialization diligence obligations, and patent prosecution and

maintenance obligations, as well as financial obligations such as potential development milestone payments, sublicensing income payments, and royalty payments. If we fail to comply with any of these obligations or otherwise breach other terms of our license agreement, and fail to cure such breach, UC may have the right to terminate the license or, in the instance where we fail to meet our diligence obligations, UC may instead elect to change our exclusive license to a non-exclusive license. The loss of the license from UC would affect a portion of the patent portfolio for OTIPRIO and OTO-413, as well as certain other product candidates we may develop. While we could still proceed with development and, if approved, commercialization of OTIPRIO, 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 and product candidates, and what activities satisfy those diligence obligations.

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

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We have received confidential and proprietary information from third parties. In addition, we employ individuals, consultants and independent contractors who were previously employed at other biotechnology or pharmaceutical companies. 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 from the FDA. Obtaining regulatory approval of a product can be a lengthy, expensive and uncertain process. In addition, failure to comply with FDA and other applicable United States and foreign regulatory requirements may subject us to administrative or judicially imposed sanctions or other actions, including:

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

Prior to obtaining approval to commercialize a product candidate in the United States or abroad, we must demonstrate with substantial evidence from well-controlled nonclinical studies and clinical trials, and to the satisfaction of the FDA or other foreign regulatory agencies, that such product candidates are safe and effective for their intended uses. Results from nonclinical studies and clinical trials can be interpreted in different ways, and insufficient or adverse results from nonclinical studies can affect the ability to conduct clinical trials. 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.

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

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

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

Our ongoing regulatory requirements may also change from time to time, potentially harming or making costlier our commercialization efforts. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or other countries. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business.

Our relationships with healthcare professionals, clinical investigators, CROs and third-party payors in connection with our current and future business activities may be subject to federal and state healthcare fraud and abuse laws, false claims laws, transparency laws, government price reporting, and 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.

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

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

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

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

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

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

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

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

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

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

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

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

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

Risks Related to Ownership of Our Securities

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

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

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 (File No. 333-227269) was declared effective by the SEC, pursuant to which we may offer debt securities, preferred stock, common stock and certain other securities from time to time. In 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.

We have agreed that for a period of 60 days after April 7, 2021, and our directors and executive officers have agreed that for a period of 60 days after April 7, 2021, subject to specified exceptions, we or they will not offer, sell, contract to sell, pledge or otherwise dispose of, directly or indirectly, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock. Sales of stock by any of our directors, executive officers or principal stockholders could have a material adverse effect on the trading price of our common stock.

On August 1, 2019, we filed a prospectus supplement in connection with an “at-the-market” offering under our 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 be further diluted 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 March 31, 2021, our executive officers, directors and current beneficial owners of 5% or more of our common stock, in aggregate, beneficially owned more than 43% 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 issue 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, 2020, we had U.S. federal and state net operating loss carryforwards (NOLs) of approximately \$382.8 million and \$124.8 million, respectively. Of our federal NOLs, approximately \$142.2 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, 2020, we had federal and California research and development tax credit carryforwards of approximately \$12.0 million and \$5.8 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. 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. In the event that it is determined that we have in the past experienced additional ownership changes, or if we experience one or more ownership changes as a result of future transactions in our stock, then we may be further limited in our ability to use our NOLs and other tax assets to reduce taxes owed on the net taxable income that we earn in the event that we attain profitability. Any such limitations on the ability to use our NOLs and other tax assets could adversely impact our business, financial condition and operating results in the event that we attain profitability.

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

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

We have incurred and will continue to incur costs as a result of operating as a public company, and our management has been and will continue to be required to devote substantial time to new compliance initiatives and corporate governance practices, including maintaining an effective system of internal control over financial reporting.

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

As a public company in the United States, we are required, pursuant to the Sarbanes-Oxley Act, to maintain effective disclosure controls and procedures and internal control over financial reporting. We are also required to provide an annual management report on the effectiveness of our disclosure controls and procedures over financial reporting. We need to disclose any material weaknesses identified by our management in our internal control over financial reporting, and at any time when we are not a non-accelerated filer, we will need to provide a statement that our independent registered public accounting firm has issued an opinion on our internal control over financial reporting. The controls and other procedures are designed to ensure that information required to be disclosed by us in the reports that we file with the SEC, is disclosed accurately and is recorded, processed, summarized and reported within the time periods specified in SEC rules and forms.

Our current controls, and any new controls that we develop may become inadequate because of changes in conditions in our business or the degree of compliance with these policies or procedures may deteriorate and significant deficiencies or material weaknesses in our internal control over financial reporting may be discovered. We may err in the design or operation of our controls, and all internal control systems, no matter how well designed and operated, may provide only reasonable assurance that the objectives of the control system are met. Because there are inherent limitations in all control systems, there can be no absolute assurance that all control issues have been or will be detected. Any failure to develop or maintain effective controls or any difficulties encountered in their implementation could harm our results of operations or cause us to fail to meet our reporting obligations and may result in a restatement of our financial statements for prior periods. Any failure to implement and maintain effective internal control over financial reporting also could adversely affect the results of periodic management evaluations regarding the effectiveness of our internal control over financial reporting that are required to be included in our periodic reports that will be filed with the SEC. Ineffective disclosure controls and procedures and internal control over financial reporting could also cause investors to lose confidence in our reported financial information and operating results, which could result in a negative market reaction and effect on the trading price of our common stock.

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

We are a "smaller reporting company," as defined in Rule 12b-2 of the Exchange Act. For as long as we remain a "smaller reporting company," we are permitted and intend to continue to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not "smaller reporting companies." These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's discussion and analysis of financial condition and results of operations" disclosure; and
- reduced disclosure obligations regarding executive compensation.

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

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 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

None.

ITEM 3. DEFAULT UPON SENIOR SECURITIES

None.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

ITEM 5. OTHER INFORMATION

None.

ITEM 6. EXHIBITS

The following is a list of exhibits filed as part of this Quarterly Report on Form 10-Q:

Exhibit Number	Description of Document	Incorporated by Reference Herein			
		Form	File No.	Exhibit	Filing Date
3.1	Amended and Restated Certificate of Incorporation of the Registrant, as amended, as currently in effect.	S-1/A	333-197365	3.2	August 1, 2014
3.2	Amended and Restated Bylaws of the Registrant.	8-K	001-36591	3.1	July 9, 2020
4.1	Form of Pre-Funded Warrant.	8-K	001-36591	4.1	April 9, 2021
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).				

+ In accordance with Item 601(b)(32)(ii) of Regulation S-K and SEC Release Nos. 33-8238 and 34-47986, Final Rule; Management's Reports on Internal Control over Financial Reporting and Certification of Disclosure in Exchange Act Periodic Reports, the Certification furnished in Exhibit 32.1 and 32.2 hereto is deemed to accompany this Form 10-Q and will not be filed for purposes of Section 18 of the Exchange Act. Such certification will not be deemed incorporated by reference into any filing under the Securities Act or the Exchange Act, except to the extent that the Registrant specifically incorporates it by reference.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: May 11, 2021

OTONOMY, INC.

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

Date: May 11, 2021

OTONOMY, INC.

By: /s/ Paul E. Cayer
Paul E. Cayer
Chief Financial and Business Officer

**CERTIFICATION OF PERIODIC REPORT UNDER SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002**

I, David A. Weber, Ph.D., certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Otonomy, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 11, 2021

/s/ David A. Weber

David A. Weber, Ph.D.

President and Chief Executive Officer

**CERTIFICATION OF PERIODIC REPORT UNDER SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002**

I, Paul E. Cayer, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Otonomy, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 11, 2021

/s/ Paul E. Cayer

Paul E. Cayer

Chief Financial and Business Officer

**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**

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), I, David A. Weber, Ph.D., President and Chief Executive Officer of Otonomy, Inc. (the "Company"), hereby certify that:

1. The Company's Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2021, to which this Certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and
2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: May 11, 2021

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

**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**

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), I, Paul E. Cayer, Chief Financial and Business Officer of Otonomy, Inc. (the "Company"), hereby certify that:

1. The Company's Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2021, to which this Certification is attached as Exhibit 32.2 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and
2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: May 11, 2021

By: /s/ Paul E. Cayer
Name: Paul E. Cayer
Title: Chief Financial and Business Officer