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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2023

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 001-36554

Ocular Therapeutix, Inc.
(Exact name of registrant as specified in its charter)

Delaware **(State or other jurisdiction of incorporation or organization)**	**20-5560161** **(I.R.S. Employer Identification No.)**
15 Crosby Drive **Bedford, MA** **(Address of principal executive offices)**	**01730** **(Zip Code)**

(781) 357-4000
(Registrant's telephone number, including area code)

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

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	**OCUL**	**Nasdaq Global Market**

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

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

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

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

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

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

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

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

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

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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

As of June 30, 2023, the aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant was approximately $405.7 million. The number of shares outstanding of the registrant's class of common stock, as of March 6, 2024: 148,627,439.

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report incorporates by reference information from the definitive Proxy Statement for the registrant's 2024 Annual Meeting of Stockholders, which is expected to be filed with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year ended December 31, 2023.

TABLE OF CONTENTS

FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “might,” “plan,” “predict,” “project,” “target,” “potential,” “goals,” “will,” “would,” “could,” “should,” “continue” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this Annual Report on Form 10-K include, among other things, statements about:

- our ongoing clinical trials, including the pivotal Phase 3 clinical trial of AXPAXLI that we initiated for the treatment of wet age-related macular degeneration, or wet AMD, and which we refer to as the SOL-1 trial; our Phase 1 clinical trials of AXPAXLI for the treatment of wet AMD; our Phase 1 clinical trial of AXPAXLI for the treatment of non-proliferative diabetic retinopathy, or NPDR, which we refer to as the HELIOS trial; our Phase 2 clinical trial of PAXTRAVA for the reduction of intraocular pressure, or IOP, in patients with primary open-angle glaucoma, or OAG, or ocular hypertension, or OHT; our Phase 2 clinical trial of OTX-DED for the short-term treatment of the signs and symptoms of dry eye disease; our clinical trial to evaluate DEXTENZA in pediatric subjects following cataract surgery; and our planned clinical trials, including our planned second pivotal clinical trial of AXPAXLI for the treatment of wet AMD, and our planned pivotal clinical trials of AXPAXLI for the treatment of NPDR;

- determining our next steps for PAXTRAVA for the treatment of patients with OAG or OHT, OTX-DED for the short-term treatment of the signs and symptoms of dry eye disease, and OTX-CSI for the chronic treatment of dry eye disease;

- our commercialization efforts for our product DEXTENZA;

- our plans to develop, seek regulatory approval for and commercialize AXPAXLI, PAXTRAVA, OTX-DED, OTX-CSI, and our other product candidates based on our proprietary bioresorbable hydrogel-based formulation technology ELUTYX;

- our ability to manufacture DEXTENZA and our product candidates in compliance with Current Good Manufacturing Practices and in sufficient quantities for our clinical trials and commercial use;

- the timing of and our ability to submit applications and obtain and maintain regulatory approvals for DEXTENZA and our product candidates;

- our estimates regarding future revenue; expenses; the sufficiency of our cash resources; our ability to fund our operating expenses, debt service obligations and capital expenditure requirements; and our needs for additional financing;

- our plans to raise additional capital, including through equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements, royalty agreements and marketing and distribution arrangements;

- the potential advantages of DEXTENZA and our product candidates;

- the rate and degree of market acceptance and clinical utility of our products;

- our ability to secure and maintain reimbursement for our products as well as the associated procedures to insert, implant or inject our products;

- our estimates regarding the market opportunity for DEXTENZA and our product candidates;

- our license agreement and collaboration with AffaMed Therapeutics Limited under which we are collaborating on the development and commercialization of DEXTENZA and our product candidate PAXTRAVA in mainland China, Taiwan, Hong Kong, Macau, South Korea, and the countries of the Association of Southeast Asian Nations;

- our capabilities and strategy, and the costs and timing of manufacturing, sales, marketing, distribution and other commercialization efforts with respect to DEXTENZA and any additional products for which we may obtain marketing approval in the future;

- our intellectual property position;

- our ability to identify additional products, product candidates or technologies with significant commercial potential that are consistent with our commercial objectives;

- the impact of government laws and regulations; and

- our competitive position.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the section captioned “Risk Factors” section, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures, licensing agreements or investments we may make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements included in this Annual Report on Form 10-K are made as of the date of this Annual Report on Form 10-K. We do not assume, and we expressly disclaim, any obligation or undertaking to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

This Annual Report on Form 10-K includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. All of the market data used in this Annual Report on Form 10-K involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. While we believe that the information from these industry publications, surveys and studies is reliable, we have not independently verified such data. The industry in which we operate is subject to a high degree of uncertainty and risk due to a variety of important factors, including those described in the section titled “Risk Factors.”

This Annual Report on Form 10-K contains references to our trademarks and service marks and to those belonging to other entities. Solely for convenience, trademarks and trade names referred to in this Annual Report on Form 10-K and the documents incorporated by reference herein may appear without the ® or ™ symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other companies' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other companies. AXPAXLI is a trade name which we use to refer to our OTX-TKI product candidate, and PAXTRAVA is a trade name which we use to refer to our OTX-TIC product candidate. The U.S. Food and Drug Administration, or FDA, has not approved either AXPAXLI or PAXTRAVA as product names.

SUMMARY OF RISKS RELATED TO OUR BUSINESS

Our business, financial condition, results of operations, future growth prospects and common stock price are subject to numerous risks and uncertainties that you should be aware of before making an investment decision, as more fully described under the heading "Risk Factors" and elsewhere in this Annual Report on Form 10-K. These risks include, but are not limited to, the following:

- We have a history of incurring significant losses. Our net losses were $80.7 million and $71.0 million for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023, we had an accumulated deficit of $697.6 million. We expect to incur operating losses over the next several years and may never achieve or maintain profitability.

- We will need substantial additional funding. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or our commercialization efforts. To the extent that we raise additional capital through the sale of equity, preferred equity or convertible debt securities, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our existing stockholders' rights as holders of our common stock. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

- If we raise additional funds through collaborations, strategic alliances, licensing arrangements, royalty agreements or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, products or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

- We have substantial indebtedness including under our secured term loan facility pursuant to our credit and security agreement with Barings Finance LLC as administrative agent, and the lenders party thereto, and in connection with the convertible notes that we issued pursuant to our note purchase agreement with Cap 1 LLC, an affiliate of Summer Road LLC. Our substantial indebtedness may limit cash flow available to invest in the ongoing needs of our business or otherwise affect our operations.

- We depend heavily on the success of DEXTENZA and our product candidates. Our ability to generate product revenues sufficient to achieve profitability is dependent on our successful commercialization of DEXTENZA for the treatment of ocular inflammation and pain following ophthalmic surgery and ocular itching associated with allergic conjunctivitis and our obtaining marketing approval for and successfully commercializing our product candidates.

- Clinical trials of our product candidates may not be successful. If we experience delays or difficulties in enrollment, serious adverse events or side effects are identified, or any other unforeseen events occur in connection with clinical trials of any of our product candidates, or if clinical trials of any of our product candidates fail to demonstrate safety and efficacy to the satisfaction of the FDA or other regulatory authorities or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of such product candidates.

- We may experience unforeseen events that could delay or prevent our ability to receive marketing approval or commercialize our product candidates. Clinical trials of our product candidates could produce negative or inconclusive results, or we could disagree with regulators regarding clinical trial results. We may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs. Enrollment in clinical trials may be slower than we anticipate. The cost of clinical trials of our product candidates may be greater than we anticipate.

- We are conducting our SOL-1 trial under a Special Protocol Assessment, or SPA, agreed to by the FDA. An SPA agreement indicates concurrence by the FDA with the adequacy and acceptability of specific critical elements of the overall protocol design for a clinical trial intended to support a future marketing application, but it does not indicate FDA concurrence on every protocol detail. Moreover, the FDA retains significant discretion in interpreting the terms of an SPA agreement and the data and results from any trial that is the subject of an SPA agreement. An SPA agreement does not ensure the receipt of marketing approval by the FDA or other regulatory authorities or that the approval process will be faster than conventional procedures.

- We may not be successful in our efforts to develop additional products and product candidates based on ELUTYX or to expand the use of ELUTYX for treating additional ophthalmic diseases and conditions.

- We have a single-site clinical and commercial manufacturing facility. We also depend from time to time on single-source suppliers for certain materials used in the manufacturing of our products and product candidates. If we have a material disruption in our manufacturing operations at this facility, or if we are unable to obtain sufficient components of our products and product candidates from our suppliers on acceptable terms or at all, we may not have sufficient quantities of our product candidates to meet our clinical trial requirements or of our product inventory to meet our commercial requirements. Such an event could delay our clinical trials or, particularly because we maintain limited commercial inventory, could reduce our product sales.

- DEXTENZA and any product candidates for which we obtain marketing approval may become subject to less favorable or unfavorable pricing regulations, third-party coverage or reimbursement practices or healthcare reform initiatives, which could harm our business. If DEXTENZA ceases to be eligible for reimbursement separate from ophthalmic surgery in the ambulatory surgical center setting, our net product revenues would decline significantly, and our ability to generate revenues from future sales of DEXTENZA would be adversely affected.

- If we are unable to establish and maintain adequate sales, marketing and distribution capabilities, maintain regulatory compliance for our manufacturing operations, obtain and maintain patent protection for or gain market acceptance by physicians, patients and third-party payors and others in the medical community of DEXTENZA or any of our product candidates for which we obtain marketing approval, or experience significant delays in doing so, our business will be materially harmed and our ability to generate revenues from product sales will be materially impaired.

- Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy.

- Our products face and, if approved, our product candidates will face competition from generic and branded versions of existing drugs, many of which have achieved widespread acceptance among physicians, payors and patients for the treatment of ophthalmic diseases and conditions. In addition, because the active pharmaceutical ingredients in our products and leading product candidates are available on a generic basis, competitors will be able to offer and sell products with the same active pharmaceutical ingredient as our products so long as these competitors do not infringe our patent rights.

- Even if we successfully obtain marketing approval for one or more of our product candidates, the approved product will be subject to ongoing review and extensive regulation.

- Our stock price is volatile and has fluctuated substantially. As a result of this volatility, our stockholders may not be able to sell their common stock at or above the price at which they purchased it. We have previously, and we may in the future, be the target of legal proceedings related to declines in our stock price.

PART I

Item 1. Business

We are a biopharmaceutical company committed to enhancing people's vision and quality of life through the development and commercialization of innovative therapies for diseases and conditions of the eye, with a specific focus on retinal disease. Our program for retinal disease is led by AXPAXLI (axitinib intravitreal implant, also known as OTX-TKI), which is based on our ELUTYX proprietary bioresorbable hydrogel-based formulation technology. We are currently conducting a pivotal Phase 3 clinical trial to evaluate AXPAXLI for the treatment of wet age-related macular degeneration, or wet AMD, which we refer to as the SOL-1 trial, and a Phase 1 clinical trial for the treatment of diabetic retinopathy. Our clinical portfolio also includes PAXTRAVA (travoprost intracameral implant, also known as OTX-TIC), which is currently in Phase 2 clinical development for the treatment of primary open-angle glaucoma, or OAG, or ocular hypertension, or OHT.

Our expertise in the formulation, development and commercialization of innovative therapies and our ELUTYX platform supported the development and launch of our first commercial drug product, DEXTENZA, a corticosteroid approved by the U.S. Food and Drug Administration, or FDA, for the treatment of ocular inflammation and pain following ophthalmic surgery and ocular itching associated with allergic conjunctivitis. We are also developing two other clinical-stage assets, OTX-DED (dexamethasone intracanalicular insert) for the short-term treatment of the signs and symptoms of dry eye disease, and OTX-CSI (cyclosporine intracanalicular insert) for the chronic treatment of dry eye disease, which we collectively refer to as our Dry Eye Programs, and several preclinical programs.

Our current products and product candidates in clinical development generally incorporate therapeutic agents that have previously received regulatory approval from the FDA, including small molecules, into ELUTYX, with the goal of providing local programmed release to tailor the duration and amount of the therapeutic agent to be delivered to the eye. We believe that our local programmed-release drug delivery technology has the potential to enable the treatment of conditions and diseases of both the front and the back of the eye and can be administered through a range of ocular modalities including intravitreal implants, intracameral implants, and intracanalicular inserts.

The hydrogel technology that underpins ELUTYX has been used in the human body since 1992 and has demonstrated its safety and effectiveness in over five million patients across five FDA-approved devices since that time. Our own approved product DEXTENZA, the first and only drug-eluting intracanalicular insert approved by the FDA, has been used in nearly 400,000 eyes since launch with reported adverse events in less than 1 in 10,000 patients. As a result, we believe that the ELUTYX technology is well tolerated.

We believe the ELUTYX technology can provide delivery solutions for durable therapies for wet AMD, non-proliferative diabetic retinopathy, or NPDR, and other diseases and conditions of the eye. The only factors that regulate the bioresorption of our ELUTYX polymer are temperature and pH of the aqueous environment. As body temperature and pH of the human aqueous environment are within a typical range for each human, and since water levels in the vitreous humor are more than sufficient to saturate our polymer matrix, we believe we can program our products and product candidates so that the polymer will be intact long-enough to deliver the active pharmaceutical ingredient and then be fully bio-resorbed when re-dosing is required. That ELUTYX does not create an acidic microenvironment, is easily eliminated from the vitreous, leaving behind no harmful byproducts, and has soft gel properties provides further support for the ELUTYX safety profile.

We currently focus on some of the largest markets in ophthalmology. According to the Market Scope 2022-2023 reports, our product candidates seek to address select indications within the retina, glaucoma, and dry eye disease areas of ophthalmology. These areas, in the aggregate, account for approximately $25.6 billion in global annual sales.

The following table summarizes the status of our key product candidates and development programs, as well as DEXTENZA. We hold worldwide exclusive commercial rights to the core technology underlying all of our product candidates in development and have not granted commercial rights to any marketing partners other than a license agreement and collaboration with AffaMed Therapeutics Limited, or AffaMed, for the development and commercialization of DEXTENZA and PAXTRAVA in the geographies agreed to between the parties.

PIPELINE AT A GLANCE

PROGRAM	THERAPEUTIC FOCUS	PRECLINICAL	EARLY/MID CLINICAL STAGE (PHASE 1 – PHASE 2)	PIVOTAL CLINICAL TRIAL STAGE (PHASE 3)	FDA APPROVAL	CURRENT STATUS/ANTICIPATED MILESTONES
AXPAXLI™ (axitinib intravitreal implant)	Wet AMD*			●		**Q1 2024** Screened first subject in SOL-1 trial
AXPAXLI (axitinib intravitreal implant)	Diabetic Retinopathy		●			**Q2 2024** 9-month data from the HELIOS Phase 1 trial
PAXTRAVA™ (travoprost intracameral implant)	Glaucoma and ocular hypertension		●			**Q2 2024** Top-line data from Phase 2 trial at ASCRS in April 2024
OTX-DED (dexamethasone intracanalicular insert)	Episodic dry eye disease		●			Phase 2 trial completed **H1 2024** Complete enrollment for trial to determine placebo comparator for the potential pivotal program
OTX-CSI (cyclosporine intracanalicular insert)	Dry eye disease		●			Phase 2 trial completed **H1 2024** Complete enrollment for trial to determine placebo comparator for the potential pivotal program
Dextenza	Post surgical ocular inflammation and pain Ocular itching associated with allergic conjunctivitis				●	Nearly 400,000 eyes treated to date **2023** Achieved $57.9M in net product revenue

*Age-related Macular Degeneration (AMD)

Our Strategy

Our strategy is to advance our pipeline of clinical assets, focusing specifically on our programs for wet AMD and NPDR, while we continue to build upon our experience in commercializing ophthalmology products. The key tactics of our strategy are:

- *Advance our AXPAXLI clinical development programs.*
    - Wet AMD: Complete enrollment of the SOL-1 trial, our first pivotal Phase 3 clinical trial of AXPAXLI for the treatment of wet AMD by the end of the first quarter of 2025. Subject to agreement with the FDA, we intend to commence screening of a second pivotal Phase 3 clinical trial, which we refer to as the SOL-2 trial, by the first quarter of 2025.
    - NPDR: Deliver topline data from our Phase 1 clinical trial of AXPAXLI for the treatment of NPDR, which we refer to as the HELIOS trial, in the second quarter of 2024. Subject to favorable topline data and agreement with the FDA, we intend to commence a pivotal Phase 3 clinical trial as a next step of clinical development.
- *Deliver topline data from our U.S.-based Phase 2 clinical trial of PAXTRAVA for the reduction of intraocular pressure, or IOP, in patients with OAG or OHT in the second quarter of 2024.*
- *Grow DEXTENZA revenues primarily through sales for the treatment of ocular inflammation and pain following ophthalmic surgery.*
- *Deliver topline data from our ongoing trial to evaluate OTX-DED in the fourth quarter of 2024.*

Limitations of Current Drug Delivery in Ophthalmology

Eye Drops

Eye drops are widely used to deliver medications directly to the ocular surface and to intraocular tissue in the front of the eye. Eye drops are administrable by the patient or care provider, inexpensive to produce and treat the local tissue. However, eye drops have significant limitations, especially when used for chronic diseases or when requiring frequent administration, including:

- *Lack of patient compliance*. Eye drops require frequent administration, and, as a result, patient compliance with required dosing regimens frequently suffers. Poor patient compliance can lead to diminished efficacy and disease progression.

- *Difficulty in administration*. Eye drops are difficult to administer for many patients, particularly among the elderly, due to physical or mental conditions such as arthritis or dementia. We believe that this also may play a large role in lack of patient compliance and resulting diminished efficacy of treatment.

- *Need for high concentrations*. After eye drops are administered to the ocular surface, the tear film rapidly renews. Most topically applied solutions are washed away by new tear fluid within 15 to 30 seconds. Because contact time with the ocular surface is short, less than 5% of the applied dose actually penetrates to reach intraocular tissues. As a result, eye drops generally require frequent administration at high drug concentrations to deliver a meaningful amount of drug to the eye. This pulsed therapy results in significant variations in drug concentrations over a treatment period, which we refer to as peak and valley dosing. At peak levels, the high concentrations can result in side effects, such as burning, stinging, redness of the clear membrane covering the white part of the eye, referred to as hyperemia, and spikes in IOP, which may lead to drug induced glaucoma. At low concentration levels, the drug may not be effective, thus allowing the disease to progress.

- *Side effects of preservatives*. To guard against contamination, many eye drops are formulated with antimicrobial preservatives, most commonly benzalkonium chloride, or BAK. Patients on long term or chronic therapy, such as glaucoma patients, often suffer reactions, which have been linked to BAK, including burning, stinging, hyperemia, irritation and eye dryness. Less frequently, conjunctivitis or corneal damage may result.

As a result of these limitations, eye drops are often suboptimal as a therapeutic option for the treatment of many diseases and conditions of the front of the eye**.**

Back-of-the-Eye Injections

An intravitreal injection is a procedure to place a medication directly into the space in the back of the eye called the vitreous cavity, which is filled with a jelly-like fluid called the vitreous humor gel. The procedure is usually performed by a trained retina specialist in the office setting. Intravitreal injections are used to administer medications to treat a variety of chronic conditions; wet AMD, diabetic retinopathy, diabetic retinal edema, or DME, and retinal vein occlusion, or RVO, are among the most common conditions treated with intravitreal anti-VEGF (vascular endothelial growth factor, or VEGFs) drugs. Anti-VEGF drugs and steroids help to reduce fluid leakage associated with these disorders.

While anti-VEGF treatment regimens can be very effective therapies, there are a number of significant drawbacks, driven primarily by the frequency of injections that typically range from every six to eight weeks. We refer to the number of injections a patient has over a given time period as the treatment burden of the particular treatment. The actual injection at the time of administration is uncomfortable for patients and can be a deterrent in terms of compliance. Then there is the burden to both patients and their caregivers of regular office visits. These patients may not be mobile enough to travel to the office on their own and therefore require not only the assistance of a caregiver but also transportation to and from the office. These patients may also be younger, part of the active workforce and therefore unwilling or unable to take personal time off to receive frequent injections. Furthermore, injecting high doses of drug to the back of the eye every four to six weeks can result in the macula constantly alternating between a thicker and a thinner state, which may lead to fibrosis presenting as scarring and atrophy. Finally, while intravitreal injections are typically safe, there is the potential risk of endophthalmitis (infection in the eye), inflammation, bleeding into the vitreous gel and retinal detachment that comes with injections.

As a result of these limitations, there is a significant unmet need for technologies that will allow for a longer duration of effect and an overall reduced number of injections.

The Ocular Therapeutix Approach

Our Hydrogel-Based Formulation Technology ELUTYX

We apply our expertise with ELUTYX to the development of products for local programmed-release of known, FDA-approved therapeutic agents for a variety of ophthalmic diseases and conditions and to ophthalmic wound closure.

ELUTYX is based on the use of a proprietary form of PEG. Our technical capabilities include a deep understanding of the polymer chemistry of PEG-based hydrogels and the design of the highly specialized manufacturing processes required to achieve a reliable, preservative-free and pure product. We tailor the hydrogel to act as a vehicle for local programmed-release drug delivery to the eye and as an ocular tissue sealant.

We create our hydrogels by cross-linking PEG molecules to form a network that resembles a three-dimensional mesh on a molecular level. Our PEG molecules are branched, with four to eight branches or arms. Each arm bears a reactive site on its end. Our cross-linking chemistry uses a second molecule with four arms, bearing complimentary reactive sites on each end, such that when combined with the PEG molecules, a network spontaneously forms. When swollen with water, this molecular network forms a hydrogel. We design these hydrogels to slowly degrade in the presence of water, a process called hydrolysis, by inserting a biodegradable linkage between the PEG molecule and the cross-linked molecule. By appropriately selecting the number of arms of the PEG molecule and the biodegradable linkage, we can design hydrogels with varying mechanical properties and bioresorption rates. Because the body has an abundance of water at a constant temperature and pH level, hydrolysis provides a predictable and reproducible degradation rate. Our technology enables us to make hydrogels that can bioresorb over days, weeks or months.

We select the active pharmaceutical ingredients for our local programmed-release drug delivery product candidates based on criteria we have developed through our extensive experience with hydrogel-based technologies. We consider the following selection criteria:

- prior approval by the FDA for the targeted ophthalmic indication, except for our AXPAXLI program in which the active pharmaceutical ingredient, axitinib, is not currently approved for an ophthalmic indication;
- expiration of relevant patent protection prior to or within our anticipated development timeline;
- high potency to minimize required drug load in the intracanalicular insert, intracameral implant or intravitreal implant;
- availability from a qualified supplier; and
- compatibility with our drug delivery system.

We believe our current and future intracanalicular insert, intracameral implant and intravitreal implant products and product candidates may offer a range of favorable attributes as compared to eye drops and immediate release back-of-the-eye injections, including:

- *Improved patient compliance*. Our inserts and implants are placed by a healthcare professional and are designed to provide local programmed-release of drug to the ocular surface, intracameral space or intravitreal space. Because patients are not responsible for self-administration of the drug and the inserts and implants dissipate over time and do not require removal for acute conditions or frequent removal for chronic conditions, we believe our inserts and implants address the problem of patient compliance.

- *Ease of administration*. We have designed our inserts and implants to provide the entire course of medication with a single administration by a healthcare professional for acute conditions or for months for chronic conditions. We believe this avoids the need for frequent administration, reducing the patient's treatment burden and the likelihood of potential complications that could result if doses are missed.

- *Local programmed-release of drug*. We have designed our inserts and implants to deliver drug in a programmed fashion in order to avoid the peak and valley dosing and related side effects and spikes in IOP associated with eye drops, as well as current standard of care injections for the back of the eye. We also believe programmed-release dosing may improve the therapeutic profile of the active pharmaceutical ingredient because it eliminates periods of little or no drug presence between eye drop or back of the eye injection administrations. Further, we are designing our products and product candidates so that their drug release profiles can be tailored or programmed to match the treatment needs of the disease. For example, steroids for ophthalmic purposes generally require administration over four weeks, with tapered dosing over this period. In contrast, PGAs require administration in a steady fashion over the duration of treatment. Our inserts and implants are designed to fully dissipate and can be removed if necessary by a healthcare professional.

- *Avoidance of preservative side effects*. Our inserts and implants do not involve the use of preservatives, such as BAK, which have been linked to side effects including burning, stinging, hyperemia, irritation, eye dryness and, less frequently, conjunctivitis or corneal damage.

Intracanalicular Inserts

Our intracanalicular inserts, including DEXTENZA, OTX-DED, and OTX-CSI, are designed to be inserted into the patient's punctum by a healthcare professional and to release drug to the surface of the eye to address diseases including ocular inflammation and pain following ophthalmic surgery, ocular itching associated with allergic conjunctivitis, and dry eye disease.

Our intracanalicular inserts utilize our proprietary hydrogel-based formulation technology and are embedded with an active drug. Following insertion through the punctum, our inserts swell in tear fluid to fill the vertical canaliculus, which secures the inserts in place. Over time, the inserts liquefy and are cleared through the nasolacrimal duct. If necessary due to excessive tearing, discomfort or improper placement, a healthcare professional can remove an intracanalicular insert by a process of pushing the soft insert back through the punctum.

Intracameral Implants

We are engaged in the clinical development of our hydrogel administered via intracameral injection to address glaucoma. Intracameral implants refer to biodegradable or bioresorbable implants placed into the anterior chamber or front of the eye for the treatment of ocular conditions. The implants are designed to be held in place by currents and gravity present in the anterior chamber of an eye. In the case of PAXTRAVA, the implant is designed to infuse with liquid, settle into the inferior angle of the eye and demonstrate little to no movement. The implants are preferably polymeric, biodegradable and provide sustained release of at least one therapeutic agent to both the trabecular meshwork and associated ocular tissue and the fluids within the anterior chamber of an eye.

Intravitreal Implants

We are engaged in the clinical development of our hydrogel administered via intravitreal injection to address the large and growing markets for diseases and conditions of the back of the eye. Our intravitreal implant product candidates, such as AXPAXLI, consist of a PEG-based hydrogel suspension, which contains embedded micronized particles of active drug. We design the intravitreal implant to be injected and retained in the vitreous humor to provide local programmed-release intravitreal delivery of anti-VEGF compounds.

Clinical Portfolio

Retinal Diseases

Age-related macular degeneration, or AMD, and diabetic retinopathy are the most common retinal diseases, affecting approximately 212.0 million and 146.4 million, respectively, worldwide, according to the Market Scope 2023 Retinal Pharmaceuticals Market Report. In the United States, Market Scope estimates that there are approximately 17.9 million suffering from some form of AMD.

Wet Aged-Related Macular Degeneration (Wet AMD)

Wet AMD is a serious disease of the central portion of the retina, known as the macula, an oval-shaped pigmented area that is responsible for detailed central vision and color perception. Wet AMD is characterized by abnormal new blood vessel formation, referred to as neovascularization, which results in blood vessel leakage and retinal distortion. If untreated, neovascularization in wet AMD patients typically results in formation of a scar under the macular region of the retina. The current standard of care for wet AMD is treatment with drugs that target VEGF, one of several proteins involved in neovascularization.

Wet AMD is the most common cause of visual impairment among elderly patients in developed countries. According to the Market Scope 2023 Retinal Pharmaceuticals Market Report, there are approximately 1.6 million people in the United States who suffer from wet AMD. This population is expected to grow at a 3.5% compound annual growth rate through 2028.

Diabetic Retinopathy (DR)

DR is a progressive condition in which chronically elevated levels of blood glucose and depleted levels of oxygen damage the tiny blood vessels in the retina. DR is among the most common microvascular complications of diabetes, making diabetes the leading cause of new cases of blindness in adults. DR can take time to develop. NPDR, sometimes called background retinopathy, is usually mild and may go unnoticed. Proliferative DR is the most serious stage of the disease and develops when areas of the retina are starved for nourishment and oxygen, triggering the proliferation of new blood vessels via secretions of VEGFs. The current standard of care for DR at the non-proliferative stage is watchful waiting, with the use of anti-VEGFs when the disease has progressed to the proliferative stage.

It is estimated that there were 8.6 million cases of DR in the United States in 2023 according to the Market Scope 2023 Retinal Pharmaceuticals Market Report, of which 3.4 million cases were moderate to severe NPDR, growing at an approximately 1.8% compound annual growth rate through 2028. Overall, there are an estimated 146.4 million cases of DR globally, growing at a compound annual growth rate of 3.1%.

Market Data

The global market for retinal disease inclusive of wet AMD and DR was approximately $16.5 billion in 2023 and is estimated to grow at approximately 6.1% per year through 2028 according to Market Scope. The U.S. market accounted for approximately 58% of the global market or $9.5 billion in 2023 and is expected to grow at approximately 5.6% through 2028.

The anti-VEGF market for the treatment of wet AMD consists predominantly of three drugs that are approved for marketing and primarily prescribed for the treatment of wet AMD: Eylea, marketed in the United States by Regeneron; Lucentis, marketed in the United States by Genentech; and Vabysmo, launched in 2022 and marketed in the United States by Genentech. Bevacizumab, also known as Avastin, an anti-VEGF therapy approved for the treatment of certain cancers, is also used off-label in ophthalmology.

Retinal Programs

AXPAXLI (axitinib intravitreal implant)

Our product candidate AXPAXLI is a preformed, bioresorbable hydrogel fiber implant based on our ELUTYX technology incorporating axitinib, a small molecule TKI with anti-angiogenic properties. AXPAXLI is delivered by intravitreal injection and is designed for a duration of six months or longer. We are conducting the SOL-1 trial to evaluate AXPAXLI for the treatment of wet AMD in the United States, Argentina, and several other countries. Subject to agreement with the FDA, we intend to commence screening of the SOL-2 trial by the first quarter of 2025. We have also conducted a Phase 1 clinical trial in Australia and a Phase 1 clinical trial in the United States to evaluate AXPAXLI for the treatment of wet AMD. We are also conducting the HELIOS trial in the United States to evaluate AXPAXLI for the treatment of NPDR. Subject to favorable topline data from the HELIOS trial and agreement with the FDA, we intend to commence a pivotal Phase 3 clinical trial of AXAPXLI for the treatment of NPDR as a next step of clinical development.

We believe axitinib is well suited for use with our platform given its high potency, multi-target capability, and compatibility with a hydrogel vehicle. In the absence of a sophisticated drug delivery system, TKIs have been difficult to deliver to the eye for acceptable time frames at therapeutic levels without causing local and systemic toxicity due to low drug solubility and very short half-lives in solution. We believe our local programmed-release drug delivery technology gives us potential advantages in this regard. Our initial implants have delivered anti-VEGF compounds *in vitro* over a targeted nine-to-twelve-month period, which we believe could make it possible to reduce patients' treatment burden by reducing the frequency of the current monthly or bi-monthly intravitreal injection regimen for wet AMD.

We conducted the two Phase 1 trials of AXPAXLI for the treatment of wet AMD with different formulations of axitinib. We are conducting the SOL-1 trial, and intend to conduct the SOL-2 trial and any pivotal trials for the treatment of NPDR, with a single 450 µg axitinib implant formulation of AXPAXLI, which is a different formulation than we used in either of the two Phase 1 trials.

Wet Age-Related Macular Degeneration (wet AMD)

The SOL-1 Trial

We initiated the SOL-1 trial, our first pivotal Phase 3 clinical trial of AXPAXLI for the treatment of wet AMD, in September 2023 with the activation of the trial's first clinical site. The SOL-1 trial is designed as a prospective, multi-center, randomized, parallel-group trial that will be run primarily at U.S. sites, as well as sites in Argentina and several other countries. The SOL-1 trial is designed as a superiority trial comparing a single optimized implant of AXPAXLI with a drug load of 450 µg of a more soluble form of axitinib to a single injection of aflibercept and assessing the safety and efficacy of AXPAXLI in subjects with wet AMD by measuring Best Corrected Visual Accuity, or BCVA, and central subfield thickness, or CSFT.

We plan to enroll approximately 300 evaluable wet AMD subjects who are treatment naïve in the study eye with good visual acuity and a diagnosis of choroidal neovascularization or sub-foveal neovascularization at screening in the SOL-1 trial. Every enrolled subject will receive two aflibercept injections between the initial screening visit and day 1: one at week -8 and another at week -4. Subjects reaching approximately 20/20 vision or experiencing an improvement of 10 Early Treatment of Diabetic Retinopathy Study, or ETDRS, letters after these injections, in addition to satisfying other enrollment criteria, will then be randomized in the trial at baseline to receive either one implant of AXPAXLI in the investigational arm or one injection of aflibercept in the control arm, followed every month and rescued as needed with supplemental anti-VEGF treatment based on pre-specified criteria. The primary endpoint is the proportion of subjects who maintained visual acuity, defined as a BCVA loss of less than 15 letters on the ETDRS chart at week 36. Our pre-specified rescue criteria are a loss of 15 or more letters on the ETDRS chart compared to baseline, or a new hemorrhage that is deemed to be likely to cause irreversible vision loss. A loss of 15 letters or more on the ETDRS chart at any time in the trial would be considered as having met the endpoint as a treatment failure.

In September 2023, we submitted a request for a Special Protocol Assessment, or SPA, to the FDA to determine whether the proposed clinical protocol and the statistical analysis plan for the SOL-1 trial adequately addressed scientific and regulatory requirements for a clinical trial that could support a marketing application. We received an agreement letter regarding the overall trial design from the FDA under the SPA on October 30, 2023. In December 2023, we submitted the SPA Agreement Modification to the FDA to broaden the inclusion criteria for subjects in the SOL-1 trial and to reflect our intention to evaluate a single optimized implant of AXPAXLI with a drug load of 450 µg of a more soluble form of axitinib in the trial. This optimized configuration is expected to provide for a slightly increased daily release of the drug and is designed to improve synchronization of axitinib drug depletion with hydrogel bioresorption. We received an agreement letter regarding the SPA Agreement Modification from the FDA on January 22, 2024. The SPA Agreement Modification enables the trial to include treatment-naïve wet AMD subjects with visual acuity of approximately 20/80 or better at the initial screening visit.

The first three subjects in the SOL-1 trial were screened and received their first aflibercept injection in February 2024. We expect to complete enrollment of the SOL-1 trial by the end of the first quarter of 2025.

Phase 1 Clinical Trial (Australia)

We have conducted an open-label, multi-center, proof-of-concept, dose-escalation Phase 1 clinical trial of AXPAXLI for the treatment of patients with wet AMD caused by excessive blood vessel growth in the back of the eye due to VEGF. This Phase 1 clinical trial was designed to evaluate the safety, durability and tolerability of AXPAXLI. All subjects have exited this Phase 1 clinical trial and we are in the process of closing all clinical sites.

Our Phase 1 clinical trial of AXPAXLI in Australia was submitted to the Therapeutic Goods Administration, Australia's regulatory authority for therapeutic goods, in July 2018 and was being conducted at multiple sites in Australia. The Phase 1 clinical trial was comprised of four cohorts consisting of subjects with pre-existing intraretinal and/or subretinal fluid: a lower dose cohort of 200 µg with six subjects; a higher dose cohort of 400 µg with seven subjects; a third cohort with two parallel arms, one arm of four subjects receiving a concomitant anti-VEGF injection with 400 µg of AXPAXLI and the other arm of six subjects receiving a 600 µg of AXPAXLI with no anti-VEGF injection; and a fourth cohort with two parallel arms, one arm of one subject receiving a 600 µg single implant of AXPAXLI and the other arm of five subjects receiving a 600 µg single implant of AXPAXLI with anti-VEGF injection. In this trial, we evaluated whether AXPAXLI can reduce existing fluid levels.

In the Phase 1 clinical trial of AXPAXLI conducted in Australia, we evaluated biological activity by measuring CSFT, using spectral domain optical coherence tomography, or OCT, and following visual acuity over time as measured by BCVA.

In February 2022, data as of January 11, 2022 from this Phase 1 clinical trial of AXPAXLI was presented at the Angiogenesis, Exudation and Degeneration Virtual Symposium. In subjects with subretinal and/or intraretinal fluid due to wet AMD, AXPAXLI was observed to be generally well tolerated. No ocular serious adverse events were reported in treatment naïve or previously treated wet AMD subjects. Plasma concentrations of the active drug (axitinib) were measured to be below the limit of quantification of assay, or BLQ < 0.1 ng/ml, at all sampled time points for all subjects in cohorts 1, 2, 3a and 3b. This assessment indicated that there was no measurable systemic exposure to axitinib.

This interim data also showed a preliminary signal of biological activity as observed by a clinically meaningful decrease in intraretinal and/or subretinal fluid as measured by high resolution OCT that provides cross-sectional images of the anatomical structure of the retina. Some subjects showed a decrease in intraretinal or subretinal fluid by two months in cohorts 2 (400 µg) and 3a (600 µg). In cohort 3b (400 µg dose plus anti-VEGF induction injection of aflibercept), two subjects showed a decrease in intraretinal or subretinal fluid as early as a week after treatment. We observed extended duration of activity of six months or more for over 60% of subjects across all cohorts and for over 80% of subjects in cohort 3a, in which we administered a 600 µg dose.

In addition, the AXPAXLI implants in cohort 1 (single implant) were observed to have biodegraded in all subjects within nine to 10.5 months of injection. It has also been observed in the trial that the implants were able to be adequately monitored and that there was limited to no movement of the implant.

Phase 1 Clinical Trial (United States)

We have conducted a prospective, multi-center, randomized, controlled Phase 1 clinical trial in the United States under an exploratory investigational new drug, or eIND, application to evaluate a single implant 600 µg dose of AXPAXLI with an anti-VEGF injection in comparison with a 2 mg dose of aflibercept. The population we studied in this U.S.-based clinical trial was different than the population we studied in our Phase 1 clinical trial of AXPAXLI in Australia. In this trial, we evaluated how long we are able to maintain subjects who have been previously treated with anti-VEGF therapy without the need for retreatment. All subjects have exited this Phase 1 clinical trial and we are in the process of closing all clinical sites.

The trial enrolled a total of 21 subjects at six clinical sites, comprising two arms consisting of subjects previously treated with, and responsive to, standard of care anti-VEGF therapy: a 16-subject arm receiving AXPAXLI in combination with a single anti-VEGF injection at month one and a five-subject arm receiving on-label aflibercept at eight-week intervals. The trial was designed to assess the safety, durability and tolerability of AXPAXLI as well as to assess preliminary biological activity in subjects by measuring anatomical and functional changes.

In February 2023, we announced interim 10-month data from the Phase 1 clinical trial of AXPAXLI in the United States at the Angiogenesis, Exudation, and Degeneration 2023 Annual Meeting. As of the December 12, 2022 cut-off date, the interim data showed that the single 600 µg AXPAXLI implant was generally well tolerated with no drug-related ocular or systemic serious adverse events, or SAEs, observed through 10 months. One SAE of endophthalmitis was observed in the AXPAXLI arm which occurred following the aflibercept injection required by the clinical trial protocol at month one and was assessed by the investigator as related to the injection procedure. There were no instances of elevated IOP, retinal detachment, retinal vasculitis, or implant migration into the anterior chamber observed in the AXPAXLI arm, and no subjects had dropped out of either arm as of the data cutoff.

The interim results showed subjects treated with a single AXPAXLI implant demonstrated stable and sustained BCVA (mean change from baseline of -0.3 letters) and CSFT (mean change from baseline of -1.3 µm) in the AXPAXLI arm at 10 months, which was comparable with the aflibercept arm (mean change from BCVA baseline of -0.8 letters; mean change from CSFT baseline of -4.5 µm). Up to Month 10, 73% of subjects remained rescue-free. Overall, a 92% reduction in treatment burden (average percent decrease in injections over the period compared to a standard monthly injection regimen) was observed in AXPAXLI treated subjects for up to 10 months. Four subjects were rescued in the AXPAXLI arm up to Month 10. One subject, the subject who experienced endophthalmitis, was rescued twice. None of these rescues met the preestablished rescue criteria set forth in the clinical trial protocol and were instead initiated at investigator discretion. One additional subject, who met the established rescue criteria at such subject’s Month 10 visit, was rescued at the end of Month 10.

There was one subject randomized to the AXPAXLI arm who was inadvertently given aflibercept instead of sham injections at the subject’s month three and month five visits. Since this subject was not treated according to protocol, the subject was excluded from the analysis of biological activity, which comprised 15 out of the 16 subjects in the AXPAXLI arm and all five subjects in the aflibercept arm, but the subject was included in the safety analysis which comprised all 16 subjects in the AXPAXLI arm and all five subjects in the aflibercept arm.

In April 2023, we presented data regarding the preclinical pharmacokinetics, or PK, of AXPAXLI and a review of the 10-month interim data from the ongoing Phase 1 clinical trial of AXPAXLI in the United States, including AXPAXLI implant resorption data to date. We augmented the results from our ongoing clinical trial with PK data in two animal models showing the uptake of axitinib from our hydrogel implant in the choroid and retinal pigment epithelium, or RPE, cells, where axitinib acts intra-cellularly to exert its VEGF receptor inhibiting effect. That data showed that clinically representative formulations of AXPAXLI delivered sustained axitinib concentrations through 12 months that were well above the IC50 for VEGFR-2 (vascular endothelial growth factor receptor) in cynomolgus monkey retina tissue and choroid/RPE tissues. This preclinical PK data aligns with the pharmacodynamics data we have observed to date in our ongoing U.S. clinical trial, namely the high proportion of rescue-free subjects up to Month 10 and suggests that AXPAXLI may provide continuous VEGF receptor inhibition, which, in turn, may support this new treatment paradigm, Treat to Maintain, in wet AMD care.

In June 2023, we presented 12-month data from the ongoing Phase 1 clinical trial of AXPAXLI in the United States at the Clinical Trials at the Summit 2023 conference sponsored by the American Society of Retina Specialists. As of the April 14, 2023 cut-off date, there were no drug-related ocular or systemic SAEs observed in the AXPAXLI arm except for the one SAE of endophthalmitis following the aflibercept injection at month one that we announced at the 10-month data readout in February 2023 and was assessed by the investigator as related to the injection procedure. There were no retinal detachment, retinal vasculitis, or implant migration into the anterior chamber adverse events observed in the AXPAXLI arm, and no subjects had dropped out of either arm as of the data cut-off. The results showed subjects treated with a single AXPAXLI implant continued to demonstrate sustained BCVA (mean change from baseline of -1.0 letters) and CSFT (mean change from baseline of +20.2 µm) in the AXPAXLI arm at 12 months, which was comparable with the aflibercept arm (mean change from BCVA baseline of +2.0 letters; mean change from CSFT baseline of -2.2 µm). Sixty percent of AXPAXLI subjects were rescue-free up to Month 12. At the Month 12 visit, an additional four of the subjects were rescued. Overall, an 89% reduction in treatment burden was observed in AXPAXLI treated subjects at 12 months. These results align with our expectation that we would see a reactivation of disease in some subjects, which we believe indicates that AXPAXLI continues to function as designed with axitinib concentrations beginning to fall below therapeutic levels after the implant bioresorbs.

Next Steps

Subject to agreement with the FDA, we intend to commence screening of the SOL-2 trial by the first quarter of 2025. The SOL-2 trial design is expected to be substantially similar to the design of the SOL-1 trial. If we were to obtain favorable results from the SOL-1 trial and the planned SOL-2 trial evaluating AXPAXLI for the treatment of wet AMD, we expect that we would submit an NDA under Section 505(b)(2) of the FDCA. See "—Government Regulation—Section 505(b)(2) NDAs" for additional information.

Non-Proliferative Diabetic Retinopathy (NPDR)

Phase 1 Clinical Trial

Given our belief in the potential applicability of AXPAXLI to other retinal diseases, we initiated the HELIOS trial to evaluate AXPAXLI for the treatment of NPDR in the fourth quarter of 2022. The HELIOS trial is a U.S.-based, multicenter, double-masked, randomized, parallel group study evaluating the safety, tolerability and biological activity of AXPAXLI in patients with moderately severe to severe NPDR without DME. We dosed our first subject in February 2023. We are conducting the Phase 1 clinical trial initially under an eIND and are in the process of converting this to a regular IND. We have enrolled 22 subjects with diabetic retinopathy secondary to type 1 or type 2 diabetes who had not had an anti-VEGF injection in the prior 12 months or diabetic macular edema in the prior six months, randomized 2:1 to either a single implant of AXPAXLI containing 600 µg of axitinib or sham control. We announced the completion of enrollment in the HELIOS trial in June 2023 and expect to provide 9-month topline data in the second quarter of 2024.

Next Steps

We have had discussions with the FDA with respect to the clinical development of AXPAXLI for the treatment of NPDR and have a potential pivotal clinical trial design that is consistent with guidance from the FDA. Subject to favorable topline data from the ongoing HELIOS trial and agreement with the FDA, we intend to commence a pivotal Phase 3 clinical trial evaluating AXPAXLI for the treatment of NPDR as a next step of clinical development.

Glaucoma

Glaucoma is a progressive and highly individualized disease in which elevated levels of IOP are associated with damage to the optic nerve, which results in irreversible vision loss. According to the World Health Organization, glaucoma is the second leading cause of blindness in the world. OHT is characterized by elevated levels of IOP without any optic nerve damage. Patients with OHT are at high risk of developing glaucoma.

In a healthy eye, fluid is continuously produced and drained to maintain pressure equilibrium and provide nutrients to the ocular tissue. Excess fluid production or insufficient drainage of fluid in the front of the eye or a combination of these problems causes increased IOP. The increased IOP associated with uncontrolled glaucoma results in degeneration of the optic nerve in the back of the eye and loss of peripheral vision. Once glaucoma develops, it is a chronic condition that requires life-long treatment.

According to the Market Scope 2023 Glaucoma Pharmaceuticals Market Report, it is estimated that there were 126.6 million people globally in 2023 with primary OAG or OHT. In the United States, it is estimated there are 6.8 million and 3.7 million who had primary OAG or OHT, respectively. Both groups are estimated to grow by 1.3% and 2.4% annually through 2026, respectively. The primary goal of glaucoma treatment is to slow the progression of this chronic disease by reducing IOP, and many medications can accomplish this. Importantly, however, adherence to current topical glaucoma therapies is known to be particularly poor with reported rates of non-adherence from 30% to 80%. These low compliance rates may be associated with disease progression and loss of vision and may be part of the reason that glaucoma is a leading cause of blindness in people over 60 years of age. Prostaglandins are the most commonly used class of medications to treat patients with glaucoma and are administered via daily eye drops as the current standard of care. The ability of patients to use and place daily eye drops is challenging. The product candidates that we are developing are designed to address the issue of compliance by delivering a prostaglandin analog, or PGA, formulated with our programmed release hydrogel to lower IOP for several months with a single insert.

Market Data

The global market for glaucoma was estimated by Market Scope at $4.3 billion in 2023 with the U.S. market representing $1.6 billion. The global market is estimated to grow at 4.9% annually to approximately $5.5 billion in 2028 while the U.S. market is expected to grow 3.9% annually to approximately $2.0 billion in 2028.

The market for drugs administered by eye drops for the treatment of glaucoma consists of both branded and generic products. Branded products have maintained premium pricing and significant market share. These products include Lumigan (bimatoprost) marketed by Allergan, Travatan Z (travoprost) marketed by Novartis, Tapros marketed by Santen, and recently approved Miebo (perfluorohexyloctane ophthalmic solution) marketed by Bausch + Lomb. Commonly used generic drugs include latanoprost and timolol.

Glaucoma Program

PAXTRAVA (travoprost intracameral implant)

Our product candidate PAXTRAVA is a bioresorbable hydrogel implant based on ELUTYX, incorporating travoprost, an FDA-approved prostaglandin analog designed to lower elevated IOP, that is designed to be administered by a physician as an intracameral injection with an initial target duration of drug release of four to six months with a single treatment.

Phase 2 Clinical Trial

We are conducting a U.S.-based Phase 2 prospective, multi-center, randomized, controlled clinical trial evaluating the safety, tolerability and efficacy of PAXTRAVA for the treatment of patients with primary OAG or OHT under an IND. The Phase 2 clinical trial was initially designed to include approximately 105 subjects at 15 to 20 sites between three arms of approximately 35 subjects each to evaluate two formulations of PAXTRAVA for the treatment of OAG or OHT in subjects compared to DURYSTA. The non-study eye of each subject receives a topical prostaglandin daily. The primary efficacy endpoint is measured by diurnal IOP mean change from baseline (8 a.m., 10 a.m. and 4 p.m.) at two, six and 12 weeks. The active comparator control arm receives one injection of DURYSTA in one eye and a topical prostaglandin daily in the non-study eye.

We initiated the Phase 2 clinical trial in the fourth quarter of 2021 and dosed the first subject in the first quarter of 2022. One arm in the Phase 2 clinical trial is receiving the same formulation used in cohort 2 of the Phase 1 clinical trial of PAXTRAVA that we conducted, containing a 26 µg dose of drug and utilizing a standard implant. The second arm was receiving the same formulation used in cohort 4 of the Phase 1 clinical trial, containing a 5 µg dose of drug and utilizing a fast-degrading implant. Due to elevations in IOP observed approximately 12 weeks after enrollment in six subjects in the PAXTRAVA 5 µg arm of the trial, we terminated enrollment in the 5 µg arm of the trial in the fourth quarter of 2022 and continued with the PAXTRAVA 26 µg and DURYSTA arms of the trial.

The Phase 2 clinical trial consists of 86 subjects: 35 subjects in the PAXTRAVA 26 µg treatment arm, 35 subjects in the DURYSTA arm and 16 subjects that were previously enrolled in the PAXTRAVA 5 µg treatment arm. Enrollment of the Phase 2 clinical trial was completed in July 2023. We have started a pilot repeat-dose sub-study in the Phase 2 clinical trial to evaluate the safety of a repeat, sustained release dose of PAXTRAVA 26 µg, in a small subset of subjects with OAG or OHT. These subjects will be followed for at least six months after their enrollment in the sub-study to monitor and evaluate their endothelial cell health. We plan to provide topline data from the single-dose portion of the Phase 2 clinical trial, assessing the safety, efficacy and durability of PAXTRAVA and whether the product candidate's preservation of endothelial cell health could make the drug suitable for chronic dosing, at the American Society of Cataract and Refractive Surgery 2024 Annual Meeting in April 2024.

Phase 1 clinical development

We submitted an IND for PAXTRAVA in February 2018 and have completed a prospective, multi-center, open-label, dose-escalation, proof-of-concept Phase 1 clinical trial of PAXTRAVA in the United States that we initiated in the second quarter of 2018 for the treatment of subjects with moderate to severe glaucoma or OHT. The clinical trial is designed to evaluate the safety, biological activity, durability and tolerability of PAXTRAVA in subjects with controlled OAG or OHT. The clinical trial consisted of four subject cohorts: cohort 1 included five subjects who received a 15 µg dose, cohort 2 included four subjects who received a 26 µg dose, cohort 3 included five subjects who received a 15 µg dose with a fast-degrading implant, and cohort 4 included five subjects who received a 5 µg dose with a fast-degrading implant.

In February 2022, at the Glaucoma 360 virtual meeting, we presented interim results from all four subject cohorts in the Phase 1 clinical trial. We believe, based on these results, that PAXTRAVA shows potential as a sustained-release therapy with a long duration of action. In the Phase 1 clinical trial, at least one subject in each of the four cohorts receiving PAXTRAVA were observed to experience a mean change in IOP from baseline as measured at 8:00 am, 10:00 a.m. and 4:00 p.m. as early as two days following injection. We believe these results were comparable to the decrease in IOP achieved with topical travoprost administered via daily eye drops, the current standard of care. IOP lowering effects lasted more than six months in subjects in cohorts 1 and 2 and three to six months in subjects in cohorts 3 and 4.

The PAXTRAVA implant was observed to biodegrade in between five and seven months in subjects in cohorts 1 and 2. In subjects in cohorts 3 and 4, the fast-degrading implants biodegraded between three and five months. Within all four cohorts, implants were not observed to move when viewed with a slit lamp biomicroscope and were visible at all examinations in all subjects using gonioscopy. Corneal health as measured by endothelial cell counts, pachymetry assessments, and slit lamp examinations did not indicate any clinically meaningful changes from baseline in any of the four cohorts. IOP elevation was observed in three subjects in cohort 3 at the approximate time of the implant resorption.

Next Steps

If the data from our Phase 2 clinical trial is favorable, we intend to evaluate our strategic alternatives for advancing the development of PAXTRAVA to pivotal Phase 3 clinical trials. If we were to decide to move the PAXTRAVA program into pivotal Phase 3 clinical trials, we would be required to successfully complete two well-controlled pivotal clinical trials conducted under an IND to seek marketing approval from the FDA. If our development efforts are successful, we expect that we would submit an NDA under Section 505(b)(2) of the FDCA. See "—Government Regulation—Section 505(b)(2) NDAs" for additional information.

Ocular Surface Diseases

Dry Eye Disease

Dry eye disease is a chronic, multifactorial disease affecting the tears and ocular surface that can result in dryness, inflammation, irritation, pain, tear film instability, visual disturbance and ocular surface damage. Dry eye disease can have a significant impact on quality of life and can potentially cause long-term damage to the ocular surface. Due to the impact of dry eye disease on tear film dynamics, the condition can affect performance of common vision-related activities such as reading, using a computer and driving, and can lead to complications associated with visual impairment. In addition, the vast majority of dry eye patients experience acute episodic exacerbations of their symptoms, which are commonly referred to as flares, at various times throughout the year. These flares can be triggered by numerous factors, including exposure to allergens, pollution, wind and low humidity, intense visual concentration such as watching television and working at a computer, hormonal changes, contact lens wear, smoking and sleep deprivation, which cause ocular surface inflammation and impact tear production and/or tear film stability.

There are approximately 17.8 million patients diagnosed with dry eye disease in the United States, according to the Market Scope 2022 Dry Eye Products Market Report. Approximately 9.8 million of those patients are diagnosed with moderate to severe dry eye while the remaining 8.0 million patients are diagnosed with mild dry eye disease. The prevalence of dry eye disease increases with age, and we expect that the number of dry eye disease cases will increase as the U.S. population continues to age.

The current standard of care for moderate to severe dry eye disease is the use of artificial tears and topical anti-inflammatory and immune modulating drugs administered by prescription eye drops. The anti-inflammatory and immune modulating prescription drug market consists of Restasis, for increasing tear production, marketed by Allergan; Cequa for increasing tear production, marketed by Sun Ophthalmics in the United States; lifitegrast, for the treatment of the signs and symptoms of dry eye disease, marketed by Bausch & Lomb (previously marketed by Novartis) under the brand name Xiidra; and off-label use of corticosteroids. As each of Restasis and Xiidra have a relatively long onset of action, they are not generally used for the short-term treatment of episodic dry eye flares. In addition, patients have reported significant issues with stinging and burning when using several of the current treatments.

Market Data

The global market for dry ocular surface disease, which we refer to as dry eye disease, was estimated by Market Scope at $5.7 billion in 2022 with the U.S. market representing $2.2 billion. There are many products to treat dry eye on the market from over an estimated 150 companies, from both the pharmaceutical and OTC segments. Within the prescription category, two of the better-known branded products are Xiidra from Novartis and Restasis from Allergan. In 2022, Xiidra recorded global sales of $487 million while Restasis recorded sales of $666 million.

Post-Surgical Ocular Inflammation and Pain

Ocular inflammation and pain are common side effects following ophthalmic surgery. Frequently performed ophthalmic surgeries include cataract, refractive, vitreoretinal, cornea, and glaucoma procedures. Physicians prescribe anti-inflammatory drugs, such as corticosteroids, which are typically administered through eye drops multiple times per day, following ocular surgery as the standard of care. These drugs improve patient comfort and also accelerate recovery through disruption of the inflammatory cascade resulting in decreased inflammation and reduced activity of the immune system. Physicians also frequently prescribe non-steroidal anti-inflammatory drugs, or NSAIDs, as adjunctive or combination therapy to supplement the use of corticosteroids. If left untreated, inflammation of the eye may result in further ocular complications, including pain, scarring and vision loss.

Market Data

Market Scope has estimated that approximately 9.8 million ocular surgeries were performed in the United States in 2023, an increase of approximately 3.5% over 2022. According to the Market Scope 2023 US and Western Europe Cataract Pharmaceuticals Market Report, there were an estimated 4.7 million cataract surgeries in the United States in 2023, an increase of 3.0% over 2022. We currently focus our sales efforts for DEXTENZA for the treatment of inflammation and pain on patients covered by Medicare Part B which accounts for roughly 50% of all cataract surgeries or approximately 2 million surgeries annually. At the current wholesale acquisition price of $555 per insert, we estimate that there is a near-term addressable market of approximately $1 billion per year in the surgical space.

According to IQVIA, Inc. data, approximately 21.6 million prescriptions were filled in the United States in 2023 for anti-inflammatory drugs administered by prescription eye drops for ocular diseases and conditions, resulting in sales of approximately $4.6 billion. These prescriptions consisted of approximately 8.8 million prescriptions and $520.0 million in sales for single-agent corticosteroids, 3.3 million prescriptions and $266.0 million in sales for NSAIDs, 5.4 million prescriptions and $348.0 million in sales for corticosteroid and antibiotic combination products and approximately 4.8 million prescriptions and $3.6 billion in sales for dry eye disease products.

Allergic Conjunctivitis

Allergic conjunctivitis, another ocular surface disease, is an inflammatory disease of the conjunctiva resulting primarily from a reaction to allergy-causing substances such as pollen or pet dander. The primary sign of this inflammation is redness and the primary symptom is acute itching. Allergic conjunctivitis ranges in clinical severity from relatively mild, common forms to more severe forms that can cause impaired vision. According to a study on the management of seasonal allergic conjunctivitis published in 2012 in the peer-reviewed journal *Acta Ophthalmologica*, allergic conjunctivitis affects 15% to 40% of the U.S. population. The first line of defense against allergic conjunctivitis is avoidance of the allergen. If this is not successful, physicians typically prescribe a combination of a topical mast cell stabilizer and an anti-histamine. These treatments act to reduce the signs and symptoms of the early phase allergic reaction. For the subset of patients with chronic or more severe forms of allergic conjunctivitis, anti-histamines and mast cell stabilizers are often not sufficient to treat their signs and symptoms. These refractory patients are frequently treated with topical corticosteroids administered by prescription eye drops.

It is estimated that up to 10 million people in the United States seek medical attention annually for the inflammatory response associated with allergic conjunctivitis caused by both seasonal and perennial allergens.

Market Data

According to IQVIA, Inc. data, approximately 4.6 million anti-allergy eye drop prescriptions were filled in the United States in 2023, resulting in sales of approximately $257.0 million. The market to treat allergic conjunctivitis consists of antihistamines, mast-cell stabilizers and steroid eye drops and consists of both branded and generic products. Commonly used branded steroids include Lotemax and Alrex (loteprednol etabonate) marketed by Bausch & Lomb, and Durezol (difluprednate) marketed by Alcon. Commonly used generic steroids include prednisolone, dexamethasone and fluorometholone.

Ocular Surface Disease Programs

We are engaged in the development of formulations of our hydrogel administered via intracanalicular inserts to address large markets for diseases and conditions of the surface of the eye. Our development efforts are focused on the use of our extended-delivery hydrogel in combination with well-known and well-understood drugs (corticosteroids and cyclosporine) for the treatment of dry eye disease, allergic conjunctivitis and inflammation and pain following ophthalmic surgery.

OTX-DED (dexamethasone intracanalicular insert)

One of the causes of dry eye disease is inflammation. Topical anti-inflammatory drugs are used as one of several therapies to treat dry eye disease and are administered by eye drops. As the understanding of dry eye disease, specifically the inflammatory components of dry eye disease, has evolved, the use of corticosteroids has become common to offer short-term relief of signs and symptoms of the disease. Physicians typically prescribe a topical corticosteroid for a period of two to four weeks, tapered over the course of delivery as the inflammation and symptoms subside. However, safety limitations associated with the prolonged use of corticosteroids for dry eye disease have limited widespread adoption. We believe that our product candidate OTX-DED has potential as a short-term treatment of the signs and symptoms of dry eye disease caused by inflammation.

OTX-DED incorporates the FDA-approved corticosteroid dexamethasone as a preservative-free active pharmaceutical ingredient in a hydrogel, drug-eluting intracanalicular insert. OTX-DED incorporates the same active drug as DEXTENZA but includes a lower dose of the drug, is administered in the office setting as a smaller insert and is designed to release dexamethasone over a period of two to three weeks, compared with up to thirty days in the case of DEXTENZA.

Phase 2 clinical trial

We submitted an IND in November 2020 for OTX-DED. In February 2021, we initiated a U.S.-based, randomized, double-masked, vehicle-controlled, multi-center Phase 2 clinical trial evaluating two different-strength formulations of OTX-DED (0.2 mg and 0.3 mg of dexamethasone) versus a hydrogel implant in a total of 166 subjects with dry eye disease, with more than 50 subjects per arm. The subjects were followed for approximately two months after randomization. This trial was designed to assess the safety and efficacy of these two formulations of OTX-DED for the short-term treatment of signs and symptoms of dry eye disease. Included subjects were required to have diagnosed dry eye disease in both eyes for at least six months, a Visual Analog Score, or VAS, eye dryness severity score of at least 30 and bulbar conjunctival hyperemia grade of at least 2 on the Cornea Contact Lens Research Unit (CCLRU) Grading scale. The primary endpoint was mean change in bulbar conjunctival hyperemia from baseline measured at 15 days post treatment by central reading center photographic assessment. Secondary endpoints included eye dryness symptoms using VAS, total CFS, or corneal total fluorescein staining, using the National Eye Institute scale and adverse events, both ocular and non-ocular.

We announced the topline Phase 2 clinical results in December 2021. The clinical trial achieved its pre-specified primary endpoint. Although the clinical trial was not powered to show statistical significance, the topline results demonstrated a statistically significant change of bulbar conjunctival hyperemia from baseline to day 15 compared to the vehicle hydrogel using a central reading photographic assessment in the modified ITT population. Change from baseline using the CCLRU Grading scale (0-4) was -0.51 for the OTX-DED 0.2 mg group (n=55), -0.43 for the OTX-DED 0.3 mg group (n=56), and -0.21 for the vehicle hydrogel insert group (n=55). These differences were statistically significant compared with the vehicle hydrogel for both the OTX-DED 0.2 mg group (p=.004) and the OTX-DED 0.3 mg group (p=.028). Sensitivity analysis using different methods of imputation including last observation carry forward (LOCF), Markov Chain Monte Carlo (MCMC), and fully conditioned specifications (FCS) were consistent with the primary analysis. Improvements from baseline were noted in the VAS dry eye symptoms for both OTX-DED 0.2 mg and OTX-DED 0.3 mg groups, but there was little separation between OTX-DED and the vehicle hydrogel insert.

Both formulations of OTX-DED were generally observed to have a favorable safety profile and be well tolerated. There were no ocular serious adverse events observed. The most common ocular adverse events for subjects treated with OTX-DED were epiphora (lacrimation increase) (8.1%) and elevated IOP (3.6%). All other ocular adverse events occurred in less than 1% of subjects. The most common non-ocular adverse event for subjects treated with OTX-DED was arthralgia (joint pain) which was seen in 1.8% of subjects. All other non-ocular adverse events occurred in less than 1% of subjects.

Ongoing Clinical Work

Based on the data from the Phase 2 clinical trial, we initiated a small trial in the second quarter of 2023 in connection with our efforts to develop an appropriate placebo comparator that may be used in both the OTX-DED and OTX-CSI programs. This trial is evaluating the performance of OTX-DED versus placebo inserts, namely fast-dissolving, biodegradable collagen plugs, and no inserts at all, to explain the placebo performance seen in the Phase 2 clinical trials evaluating both OTX-DED and OTX-CSI in which the vehicle hydrogel placebo insert or placebo comparator vehicle remained in the canaliculus longer than anticipated, performing more like an active comparator than a placebo. We anticipate we will complete enrollment for this trial in the first half of 2024, and to deliver topline data in the fourth quarter of 2024. We plan to use the results of this trial to inform the next steps for both the OTX-DED and OTX-CSI programs.

Next Steps

If the data from the ongoing trial of evaluating OTX-DED versus potential comparators is favorable, we intend to evaluate our strategic alternatives for advancing the development of OTX-DED.

OTX-CSI (cyclosporine intracanalicular insert)

OTX-CSI incorporates the FDA-approved immunomodulator cyclosporine as a preservative-free active pharmaceutical ingredient into a hydrogel, drug-eluting, intracanalicular insert. The product candidate is designed for subjects suffering from moderate to severe dry eye and to be administered by a physician as a bioresorbable intracanalicular insert. OTX-CSI is designed to release cyclosporine to the ocular surface for approximately three to four months in order to increase tear production for the chronic treatment of dry eye disease.

Phase 1 clinical development

We submitted an IND for OTX-CSI in the United States in December 2019 and initiated a Phase 1 clinical trial in the first quarter of 2020. The Phase 1 clinical trial was a U.S.-based, open-label, single-center trial that included five subjects (ten eyes) who were followed for approximately four months. The study was designed to evaluate the safety, tolerability and durability of OTX-CSI and assess the biological activity by measuring signs and symptoms of dry eye disease over this time period.

On October 8, 2020, we announced topline data from our Phase 1 clinical trial evaluating OTX-CSI in the chronic treatment of dry eye disease. All subjects completed the 16-week study period with no drop-outs. There were no serious adverse effects reported. The inserts were observed to be well-tolerated, and there were no adverse events of stinging, irritation, blurred vision or tearing reported or observed.

Tear production as measured by the Schirmer’s test improved from mean values of 4.2 mm at baseline to 8.2 mm at Week 12. One of five subjects (20%) had a greater than 10 mm increase from baseline in Schirmer’s score at Week

12. Subjects saw an improvement in signs of dry eye disease as measured by CFS (a mean value of 6.7 at baseline, improved to a mean value of 2.7 at Week 12, on a scale of 0 to 15). Further, subjects saw an improvement in symptoms of dry eye disease as measured by the VAS eye dryness severity score (a mean value of 51 at baseline, improved to a mean value of 33 at Week 12, on a scale of 0 to 100) and the VAS dry eye frequency score (a mean value of 51 at baseline, improved to a mean value of 31 at Week 12, on a scale of 0 to 100). The onset of action of OTX-CSI was seen as early as two weeks for both signs and symptoms of dry eye disease and was observed to continue over the sixteen-week study period.

Phase 2 clinical development

In September 2020, we dosed the first subjects in a U.S.-based, randomized, double-masked, multi-center, vehicle-controlled Phase 2 clinical trial designed to assess the safety, tolerability and durability and to evaluate the efficacy of OTX-CSI in the chronic treatment of dry eye disease. The Phase 2 clinical trial evaluated two different formulations of OTX-CSI compared with a hydrogel vehicle insert in approximately 140 subjects who were followed for a period of 16 weeks (12-week study period, with an additional 4-week safety follow-up). Included subjects must have been diagnosed with dry eye disease in both eyes for a period of greater than six months and have a VAS eye dryness severity score of greater than 30. The primary endpoints are incidence of treatment-emergent adverse events and the absolute value and change from baseline at week 12 in tear production as measured by the Schirmer's test. Secondary endpoints include signs of dry eye disease as measured by CFS and symptoms of dry eye disease as measured by the VAS eye dryness severity score and the VAS dry eye frequency score.

We announced topline results from our Phase 2 clinical trial in October 2021. In the Phase 2 clinical trial, OTX-CSI was administered to 147 subjects with dry eye disease at 15 sites in the United States. The four groups evaluated in this study were: OTX-CSI for a shorter duration (two to three months formulation-F1, n=42), OTX-CSI for a longer duration (three to four months formulation-F2a, n=40), vehicle insert for a longer duration (three to four months formulation-F2b, n=43) and vehicle insert for a very short duration (one week formulation-F3, n=22).

The study did not show separation between subjects receiving OTX-CSI (both formulations) and subjects receiving the vehicle (both formulations) for the primary endpoint of increased tear production at 12 weeks as measured by the Schirmer's Test. Mean change from baseline (improvement) in Schirmer's Test scores for the four groups were as follows: OTX-CSI F1: 1.98 mm, OTX-CSI F2a: 1.91 mm, Vehicle F2b: 2.24 mm and Vehicle F3: 3.08 mm.

The study did show an improvement compared with baseline in signs of dry eye disease as measured by total CFS and symptoms of dry eye disease as measured by the VAS eye dryness in subjects treated with the OTX-CSI insert (both formulations) starting as early as two weeks after insertion and continuing over the 12 weeks study period. These improvements were not statistically significant compared with vehicle insert (both formulations) for either CFS or VAS eye dryness (severity and frequency) at 12 weeks.

Overall, the OTX-CSI insert (both formulations) was generally observed to have a favorable safety profile and be well tolerated. There were no ocular serious adverse events observed. No subjects dropped out of the trial due to an adverse event. The most common ocular adverse event was ocular pruritis, or itchy eyes, which was seen in less than 16% of subjects. The adverse events of ocular discomfort or pain were seen in less than 3% of subjects. The most common non-ocular event was COVID-19 and was seen in 3% of subjects.

Next Steps

If the data from the ongoing trial of evaluating OTX-DED versus potential comparators is favorable, we intend to evaluate our strategic alternatives for advancing the development of OTX-CSI.

Commercial Portfolio

Post-Surgical Ocular Inflammation and Pain

DEXTENZA (dexamethasone intracanalicular insert)

DEXTENZA incorporates the FDA-approved corticosteroid dexamethasone as a preservative-free active pharmaceutical ingredient into a hydrogel, drug-eluting intracanalicular insert. Following FDA approval, we commercially launched DEXTENZA for the treatment of post-surgical inflammation and pain in July 2019. DEXTENZA is the first FDA-approved intracanalicular insert delivering dexamethasone to treat post-surgical ocular inflammation and pain for up to 30 days with a single administration.

We selected dexamethasone as the active pharmaceutical ingredient for DEXTENZA because it is approved by the FDA and has a long history of ophthalmic use; is available on a generic basis; is highly potent and is typically prescribed for prevention of ocular inflammation and pain following ocular surgery; is available from multiple qualified suppliers; and has physical properties that are well suited for incorporation within our hydrogel technology.

The dexamethasone drug particles embedded within our DEXTENZA intracanalicular insert gradually erode and release the drug in a programmed fashion until the drug is depleted. As the dexamethasone drug particles erode and the hydrogel degrades by hydrolysis, the intracanalicular insert softens, liquefies and is cleared through the nasolacrimal duct. We provide the DEXTENZA drug product in a preservative-free formulation in a sterile, single use package.

The standard regimen for dexamethasone eye drops following cataract surgery is an initial administration of four times daily for one week, with a gradual tapering in the number of eye drops over a four-week period. Such a regimen is often confusing to patients as they must remember to taper the number of times per day they administer the steroid, while also taking multiple drops of other drugs, such as antibiotics and NSAIDs. We believe that local programmed-release of drug to the eye may result in better control of ocular inflammation and pain as compared to prescription eye drops and that a low dose amount may provide enhanced safety by eliminating spikes in IOP associated with high-dose steroid eye drops.

Investigator-Initiated Trials

We have received proposals for, and are supporting, several investigator-initiated trials evaluating DEXTENZA in different clinical situations. To date, third-party clinical investigators have initiated over 45 trials to study the use of DEXTENZA in cataract surgery, other ophthalmic surgeries and other potential indications. Over 25 of the trials have completed enrollment, and the remaining trials are actively enrolling and treated subjects are being followed. To date, 19 of the trials have published study reports.

Post-Approval Studies

In September 2020, we announced that we had dosed the first pediatric subjects in a U.S.-based, randomized, multicenter Phase 3 clinical trial evaluating DEXTENZA for the treatment of post-surgical ocular inflammation and pain in children following cataract surgery. This clinical trial is a post-approval requirement of the FDA in accordance with the Pediatric Research Equity Act of 2003, in connection with the FDA's prior approval of DEXTENZA for the treatment of inflammation and pain following ophthalmic surgery in adults. We enrolled 65 subjects in this clinical trial. It is designed to evaluate the safety of DEXTENZA compared to an active control, prednisolone acetate suspension eye drops, for the treatment of inflammation and pain following ocular surgery for pediatric cataract in children between zero and five years of age. The FDA has agreed that this Phase 3 clinical trial evaluating DEXTENZA for the treatment of post-surgical ocular inflammation and pain in children following cataract surgery may also satisfy the post-approval requirement for a pediatric trial as it relates to the indication for ocular itching associated with allergic conjunctivitis.

All subjects have exited this trial and we are in the process of analyzing the final data. We anticipate that we will submit the clinical study report and updated package insert to the FDA in the second quarter of 2024.

Foreign Approvals

Outside the United States, we continue to assess whether to seek regulatory approval for DEXTENZA in markets such as the European Union, Australia and Japan based on the market opportunity, particularly pricing, and the requirements for marketing approval. Given our prioritization of the clinical development of our sustained-release product candidates and our planned commercialization efforts for our initial intracanalicular insert product candidates in the United States, we will need to engage third parties to assist us in the approval process.

We have entered into a license agreement and collaboration with AffaMed for the development and commercialization of DEXTENZA, along with PAXTRAVA in mainland China, Taiwan, Hong Kong, Macau, South Korea, and the countries of the Association of Southeast Asian Nations, or the AffaMed License Agreement. In January 2022, AffaMed dosed its first subject in a study conducted in China evaluating the safety and efficacy of DEXTENZA for the treatment of ocular inflammation and pain post-cataract surgery. This prospective, single-arm, real-world trial is designed to assess the safety and efficacy of DEXTENZA for the treatment of ocular inflammation and pain following cataract surgery in approximately 120 subjects at the Bo'ao Super Hospital, or the Bo'ao Real World Study. The Bo'ao Real World Study's primary efficacy endpoint is the absence of anterior chamber cells in the study eye at Day 14, and the key secondary endpoint is the absence of pain in the study eye at Day 8. In October 2023, AffaMed announced positive topline results from the Bo'ao Real World Study. As announced by AffaMed, the trial met its primary endpoint, with DEXTENZA demonstrating a significant reduction of ocular inflammation as measured by the absence of anterior chamber cells (i.e. score of "0") in the study eye on Day 14 after cataract surgery. AffaMed also announced that the trial also met its secondary endpoint, demonstrating a significant reduction of ocular pain on Day 8, and that DEXTENZA was well-tolerated and had a favorable safety profile consistent with all prior trials.

In April 2023, AffaMed announced that China's National Medical Products Administration, or NMPA, had approved AffaMed's Clinical Trial Application to initiate a Phase 3 registrational study in China to investigate the efficacy and safety of DEXTENZA in subjects following ophthalmic surgery, or the Phase 3 Registrational Study. In September 2023, AffaMed announced that the first subject had been treated in the Phase 3 Registrational Study.

In February 2024, AffaMed announced that the Singapore Health Sciences Authority has accepted AffaMed's new drug application for DEXTENZA for the treatment of ocular inflammation and pain following ophthalmic surgery, and ocular itching associated with allergic conjunctivitis for evaluation. In April 2022, AffaMed announced that DEXTENZA has been approved in Macau, China for the treatment of ocular inflammation and pain following ophthalmic surgery. We do not expect that DEXTENZA sales in Macau will result in material revenues to us.

We retain the right to develop and commercialize DEXTENZA in all other global markets. From time to time, we may consider additional arrangements with other companies to address markets outside of the United States. If we or our collaborators obtain regulatory approval to market and sell DEXTENZA in international markets, we expect to utilize a variety of types of collaboration, distribution and other marketing arrangements with one or more third parties to commercialize DEXTENZA. See "—Government Regulation—Review and Approval of Medical Devices in the European Union" for additional information.

Allergic Conjunctivitis

DEXTENZA (dexamethasone ophthalmic insert) for the Treatment of Ocular Itching Associated with Allergic Conjunctivitis

In October 2021, the FDA approved our supplemental New Drug Application, sNDA, for DEXTENZA to include the treatment of ocular itching associated with allergic conjunctivitis as an additional indication. With the approval, DEXTENZA became the first, FDA-approved, physician-administered intracanalicular insert capable of delivering a preservative-free drug for the treatment of ocular itching associated with allergic conjunctivitis with a single administration for up to 30 days. DEXTENZA for the treatment of ocular itching associated with allergic conjunctivitis also represents our first indication approved to be administered in a physician's office during a routine, non-surgical appointment.

Although dexamethasone is clinically effective in the treatment of late-phase inflammatory allergic reactions, the safety limitations associated with eye drop administration, including the potential to generate spikes in IOP due to the high levels of drug due to potential patient abuse to treat this symptomatic condition, have limited its widespread adoption. These elevations in IOP can lead to drug-induced glaucoma, although the incidence is low. Further, use of oral antihistamine medications as well as anti-histamine eye drops for allergic conjunctivitis may dry out the eye and exacerbate the discomfort to some patients. Based on our clinical trial results to date, we believe that using DEXTENZA for allergic conjunctivitis can create a low, tapered, consistent dose of dexamethasone, potentially minimizing or eliminating side effects associated with the eye drop formulation, while retaining the drug's anti-inflammatory effects.

We believe that allergic conjunctivitis represents a discrete potential market opportunity for preservative-free DEXTENZA because it is a physician-administered, hands-free, therapy administered in the office setting. We believe that many of the specialists who treat patients for post-surgical inflammation and pain also treat patients suffering from allergic conjunctivitis.

We commercially launched DEXTENZA for the treatment of ocular itching associated with allergic conjunctivitis in the first quarter of 2022 utilizing a small, dedicated and highly focused sales force of four key account managers and two field reimbursement managers that called exclusively on the offices of ophthalmologists and optometrists. In the fourth quarter of 2022, we redeployed this small sales force to join the DEXTENZA sales force focused on the ophthalmic surgery market, specifically cataract surgery, in ambulatory surgery centers, or ASCs, and hospital outpatient departments, or HOPDs. We believe that cataract surgeries represent a larger, near-term market opportunity.

AffaMed License Agreement

Under the terms of the AffaMed License Agreement, we received an upfront payment of $12 million and became eligible to receive development, regulatory and commercial milestone payments and clinical development support payments of up to $91 million in the aggregate, as well as royalties from future product sales. In the fourth quarter of 2021, we received a $1 million milestone payment upon the approval by the FDA of an sNDA for DEXTENZA to include the treatment of ocular itching associated with allergic conjunctivitis as an additional indication; in the second quarter of 2022, we received a $2 million clinical support payment in connection with dosing the first subject in a Phase 2 clinical trial evaluating PAXTRAVA for the treatment of OAG or OHT; and in the second quarter of 2023, we received a $1 million milestone payment upon the NMPA's approval of AffaMed's Phase 3 Registrational Study. Royalties are tiered and will range from the low teens to low twenty percent range. In return, we agreed to grant AffaMed exclusive rights to develop and commercialize DEXTENZA for the treatment of post-surgical inflammation and pain following ophthalmic surgery and ocular itching in patients with allergic conjunctivitis, and PAXTRAVA for the reduction of elevated IOP in patients with primary OAG or OHT in specified Asian markets. We retain the right to develop and commercialize DEXTENZA and PAXTRAVA in all other global markets.

Sales, Marketing and Distribution

We generally expect to retain commercial rights in the United States to any of our product candidates for which we may receive marketing approvals and which we believe we can successfully commercialize. In general, if we receive approval to market any of our product candidates in the United States, we plan to then evaluate the regulatory approval requirements and commercial potential for any such product candidate in Europe, Japan and other selected geographies. If we decide to commercialize our products outside of the United States, we expect to utilize a variety of types of collaboration, distribution and other marketing arrangements with one or more third parties to commercialize any product of ours that receives marketing approval.

We sell DEXTENZA in the United States primarily to a network of specialty distributors on a direct basis, who then resell DEXTENZA to ASCs, HOPDs, and physicians' offices. We also sell DEXTENZA on a direct basis to a small number of ASCs. We intend to offer this distribution option more broadly to our end customers starting in the third quarter of 2024.

In addition to distribution agreements with specialty distributors and a small number of ASCs, we enter into arrangements with government payors that provide for government-mandated rebates and chargebacks with respect to the purchase of DEXTENZA. We have built a highly targeted, key account sales force of KAMs, or key account managers, Regional Directors, and FRMs, or field reimbursement managers, that focus on the ASCs and their affiliates responsible for the largest volumes of cataract surgery in the United States, with an initial emphasis on the approximately two million cataract procedures performed annually under Medicare Part B.

During 2022, we adjusted our discounting and rebate strategy to meet the demands of the market. In the third quarter of 2022, we implemented an off-invoice discount program whereby providers receive the discounted price immediately upon purchase, rather than having to wait until the end of the quarter for a rebate payment. We focus our sales efforts on sales to ASCs and strategic accounts that own and control multiple ASCs. In the first quarter of 2023, we launched a Commercial Assurance Program to provide assistance with patients' out-of-pocket costs, supporting the expansion of DEXTENZA for commercially insured patients not covered by government payors.

Manufacturing

We fabricate devices and drug products for use in our clinical trials, research and development and commercial efforts for all of our products and product candidates using current Good Manufacturing Practices, or cGMP, at our approximately 20,000 square foot facility located in Bedford, Massachusetts. In June 2016, we entered into a new lease agreement for approximately 71,000 square feet of a facility in Bedford, Massachusetts that primarily houses our research and development functions but may include additional manufacturing space in the future.

We purchase active pharmaceutical ingredient drug substance from independent suppliers on a purchase order basis for incorporation into our drug product candidates. We purchase our PEG and other raw materials from different vendors on a purchase order basis according to our specifications. While we believe that multiple vendors are available for each component we purchase, we have historically sole-sourced each component. We qualify vendors according to our quality system requirements. We do not have any long-term supply agreements in place for any raw materials or drug substances. We do not license any technology or pay any royalties to any of our drug or raw material vendors for the current or potential front and back-of-the-eye products.

We believe that our strategic investment in manufacturing capabilities allows us to advance product candidates at a more rapid pace and with more flexibility than a contract manufacturer, although we will continue to evaluate outsourcing unit operations for cost advantages. Our manufacturing capability also enables us to produce products in a cost-effective manner while retaining control over the manufacturing process and prioritizing the timing of internal programs.

Our manufacturing capabilities encompass the full manufacturing process through quality control and quality assurance and are integrated with our project teams from discovery through development and commercial release. This structure enables us to efficiently transfer research stage product concepts into manufacturing. We have designed our manufacturing facility and processes to provide flexibility for the manufacture of different product candidates. We outsource sterilization services for our products.

We believe that we can scale our manufacturing processes to support DEXTENZA sales as well as development of our drug product candidates and the potential commercialization of such product candidates.

Intellectual Property

Our success depends in part on our ability to obtain and maintain proprietary protection for our products, product candidates, technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. We rely on patent protection, trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position.

We have issued patents and/or patent applications pending for all of our commercial products and product candidates, as well as trade secrets to protect proprietary manufacturing processes. As of December 31, 2023, we owned or exclusively licensed in certain fields of use over 250 issued U.S. patents, pending U.S. patent applications, issued foreign patents and pending foreign patent applications.

Certain of our U.S. patents and applications, and foreign counterparts, are owned by us and other U.S. patents and applications, and their foreign counterparts have been in-licensed from Incept.

The existence of patent applications does not guarantee that a patent will issue, or that any patent that does issue will cover the product or product candidate. Issued patents are subject to validity, enforceability and infringement challenges by third parties with uncertain chances of success.

The term of individual patents depends upon the legal term for patents in the countries in which they are granted. In most countries, including the United States, the patent term is generally 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country. In the United States, a patent's term may, in certain cases, be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the United States Patent and Trademark Office in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over a commonly owned patent or a patent naming a common inventor and having an earlier expiration date. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration date of a U.S. patent for certain patents as partial compensation for the length of time the drug is under regulatory review while the patent is in force. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended.

Similar provisions are available in the European Union and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our product candidates receive approval by the FDA or foreign regulatory authorities, where applicable, we expect to apply for patent term extensions on certain issued patents covering those products, depending upon the length of the clinical trials for each drug and other factors. The expiration dates referred to above are without regard to potential patent term extension or other market exclusivity that may be available to us.

We may rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements with our employees, and certain consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data.

The following is a summary of patents and patent applications that cover our commercial products and potentially cover our product candidates:

AXPAXLI (axitinib intravitreal implant) for Wet AMD, DME and RVO

We own issued patents in the United States and patents in certain foreign jurisdictions that cover this product candidate, with current expiration dates in 2041. Additional U.S. and foreign patent applications are pending.

PAXTRAVA (travoprost intracameral implant) for OAG or OHT

We have licenses to pending U.S. applications and certain foreign patent applications pending that potentially cover this product candidate that, if granted, are expected to expire in 2037. Certain foreign licensed patent applications have been issued and expire in 2037. We own an issued patent in the United States and patents in certain foreign jurisdictions that cover this product candidate, with current expiration dates in 2041. Additional owned U.S. and foreign patent applications are pending.

OTX-DED (dexamethasone intracanalicular insert) for episodic dry eye disease

We have licenses to U.S. patents, and certain foreign counterparts, with current expiration dates in 2030. We own an issued patent that expires in 2037 that covers this product candidate and a pending patent application in the United States, and certain foreign counterparts, with the potential to cover this product candidate that, if granted, are expected to expire in 2041.

OTX-CSI (cyclosporine intracanalicular insert) for dry eye disease

We have licenses to U.S. patents, and certain foreign counterparts, that cover this product candidate, with current expiration dates in 2030. We own issued patents and pending patent applications in the United States that cover this product candidate with current expiration dates in 2037 and in 2041, and corresponding foreign patent applications that, if granted, are expected to expire in 2041.

DEXTENZA (dexamethasone ophthalmic insert) 0.4 mg

We have licenses to U.S. patents, and certain foreign counterparts, with current expiration dates in 2030 that cover this product.

We also own a U.S. patent that covers this product with a current expiration date in 2037.

DEXTENZA (dexamethasone ophthalmic insert) 0.4 mg for allergic conjunctivitis

We have licenses to U.S. patents, and certain foreign counterparts, with current expiration dates in 2030 that cover this product. We also own a U.S. patent that covers this product with a current expiration date in 2037 and a pending patent application in the United States, and certain foreign counterparts, with the potential to cover this product candidate that, if granted, is expected to expire in 2041.

ReSure Sealant

We have licenses to two U.S. patents that cover ReSure Sealant. One U.S. patent is expected to expire in 2024 and relating to the process of making and using hydrogel compositions, and one U.S. patent is expected to expire in 2032 and relates to certain features of the ReSure Sealant package.

Licenses

Incept, LLC

In January 2012, we entered into an amended and restated license agreement, which we refer to as either the Prior Agreement or Original License, with Incept under which we hold an exclusive, worldwide, perpetual, irrevocable license under specified patents and technology owned or controlled by Incept to make, have made, use, offer for sale, sell, sublicense, have sublicensed, offer for sublicense and import, products delivered to or around the human eye for diagnostic, therapeutic or prophylactic purposes relating to all human ophthalmic diseases or conditions. This license covers a significant portion of the patent rights and the technology for DEXTENZA, ReSure Sealant and our hydrogel platform technology product candidates. The agreement supersedes an April 2007 license agreement between us and Incept. Amar Sawhney, our former President and Chief Executive Officer and former Executive Chairman of the Board of Directors, is a general partner of Incept.

On September 13, 2018, or the Effective Date, we entered into a second amended and restated license agreement, or the Second Amended Agreement, with Incept. The Second Amended Agreement amends and restates in full the Prior Agreement, to expand the scope of our intellectual property license and modify future intellectual property ownership and other rights thereunder.

License Rights; Ownership of Intellectual Property. We and Incept have agreed to expand the field of use of the exclusive, worldwide, perpetual, irrevocable license held by us under the Prior Agreement to include specified intellectual property rights and technology owned or controlled by Incept to make, have made, use, offer for sale, sell, sublicense, have sublicensed, offer for sublicense and import, (i) consistent with the Prior Agreement, products delivered to or around the human eye for diagnostic, therapeutic or prophylactic purposes relating to all human ophthalmic diseases or conditions, or the Ophthalmic Field of Use, and (ii) as a result of the expansion of the scope of the Original License, products delivered for the treatment of acute post-surgical pain or for the treatment of ear, nose and/or throat diseases or conditions, subject to specified exceptions, or the Additional Field of Use. We and Incept have further agreed to expand the field of use of the Original License for certain patents, patent applications and other rights pertaining to shape-changing hydrogel formulations thereunder, or the Shape-Changing IP, to include all fields except those involving the nerves and associated tissues specified in the Second Amended Agreement.

We will solely own, without a license to Incept, all intellectual property rights conceived solely by one or more individuals from our company, or the Company Individuals, after the Effective Date, subject to exceptions specified therein. Subject to certain exceptions specified in the Second Amended Agreement, Incept will own and license to the us (i) all intellectual property rights included in the Original License, or the Original IP, in the Ophthalmic Field of Use and the Additional Field of Use, (ii) intellectual property rights in the field of drug delivery conceived solely by the Company Individuals on or before the Effective Date, or Incept IP, and (iii) intellectual property rights in the field of drug delivery conceived by one or more Company Individuals jointly with one or more individuals from Incept, including Dr. Sawhney, or the Incept Individuals, after the Effective Date. These intellectual property rights are referred to as Joint IP, and, collectively with the Original IP and the Incept IP, as the Licensed IP.

Financial Terms. We and any of our sublicensees are obligated to pay Incept royalties as follows under the Second Amended Agreement: (i) consistent with the Prior Agreement, a royalty equal to a low single-digit percentage of net sales by us or our affiliates of products, devices, materials, or components thereof, or Licensed Products, including or covered by Original IP, excluding the Shape-Changing IP, in the Ophthalmic Field of Use; (ii) a royalty equal to a mid-single-digit percentage of net sales by us or our affiliates of Licensed Products including or covered by Original IP, excluding the Shape-Changing IP, in the Additional Field of Use; and (iii) a royalty equal to a low single-digit percentage of net sales by us or our affiliates of Licensed Products including or covered by Incept IP or Joint IP in the field of drug delivery. Royalty obligations under the Second Amended Agreement commence with the first commercial sale of a Licensed Product described above and terminate upon the expiration of the last-to-expire patents included in the Licensed IP, as applicable. Any sublicensee of us also will be obligated to pay Incept royalties on net sales of Licensed Products made by it and will be bound by the terms of the Second Amended Agreement to the same extent as us. Additionally, at its sole discretion, Incept may require, as a condition of any sublicense by us in the Additional Field of Use and in exchange for a reduction in the royalties owed on net sales of Licensed Products described above, payments equal to a mid-teen percentage of any upfront payment and, subject to certain conditions, other payments received by us from the sublicensee.

Patent Prosecution and Litigation. Incept will continue to have sole control and responsibility for ongoing prosecution of patents included in the Original IP, and we will have sole control and responsibility for ongoing prosecution of patents and patent applications included in or arising under the Incept IP or Joint IP. The parties have agreed to work together in good faith to enter into a separate agreement under which, subject to certain limitations, we would assume control of the prosecution of patents and patent applications included in or arising under the Shape-Changing IP. We have the right, subject to certain conditions, to bring suit against third parties who infringe the patents included in the Original IP in the Ophthalmic Field of Use or the Additional Field of Use, patents included in the Incept IP in the drug delivery filed, patents included in the Joint IP in the drug delivery field, and patents included in the Shape-Changing IP in all fields except as described above. We have also agreed, if requested by Incept, to enter into a joint defense and prosecution agreement for the purpose of allowing the parties to share confidential and attorney-client privileged information regarding the possible infringement of one or more patents covered by the Second Amended Agreement. We are responsible for all costs incurred in prosecuting any infringement action it brings.

Term and Termination. The Second Amended Agreement will expire on the later of (i) the expiration or disclaimer by us of the last valid claim of an issued and unexpired patent included in the Licensed IP or (ii) the final unappealable rejection or abandonment of the last pending patent application arising under the Licensed IP. Either party may terminate the Second Amended Agreement in the event of the other party's insolvency, bankruptcy, or comparable proceedings, or if the other party materially breaches the agreement and does not cure such breach during a specified cure period.

AffaMed License Agreement

On October 29, 2020, we entered into the AffaMed License Agreement with AffaMed for the development and commercialization of DEXTENZA regarding ocular inflammation and pain following cataract surgery and allergic conjunctivitis, or collectively, the DEXTENZA Field, and for PAXTRAVA, or collectively with DEXTENZA, the AffaMed Licensed Products, regarding OAG and OHT, or collectively, the TIC Field and, with the DEXTENZA Field, each a Field, in each case in mainland China, Taiwan, Hong Kong, Macau, South Korea, and the countries of the Association of Southeast Asian Nations, or collectively, the Territories. We retain development and commercialization rights for the AffaMed Licensed Products in the rest of the world.

Under the AffaMed License Agreement, we granted AffaMed (i) a non-exclusive, royalty-free, non-sublicensable license under certain of our intellectual property rights and know-how to use the AffaMed Licensed Products in connection with specified activities in accordance with a development plan agreed between the parties and (ii) an exclusive, royalty-bearing, sublicensable, non-transferable (subject to specified exceptions), license under certain of our intellectual property rights and know-how to commercialize the AffaMed Licensed Products in the applicable Field in the Territories. We have further agreed not to, and to cause its affiliates or agents not to, develop or commercialize in the Territories (i) the AffaMed Licensed Products outside of the applicable Fields and (ii) any other product containing the same active pharmaceutical ingredients as the AffaMed Licensed Products and administered into the anterior chamber of the eye, in each case without AffaMed's prior written consent. AffaMed has agreed not to, and to cause its affiliates or agents not to, engage in the development, manufacture, or commercialization of any competing product in the Territories.

Under the terms of the AffaMed License Agreement, we received upfront payments and we also became eligible to receive additional payments upon the achievement of certain development and commercial milestones. There can be no guarantee, however, that any of the remaining milestones will be achieved. We are also entitled to receive tiered, escalating royalties on the net sales of the AffaMed Licensed Products ranging from a low-teen to low-twenties percentage. Royalties under the AffaMed License Agreement are payable on an AffaMed Licensed Product-by-AffaMed Licensed Product and jurisdiction-by-jurisdiction basis and are subject to potential reductions in specified circumstances, subject to a specified floor.

Pursuant to the terms of the AffaMed License Agreement, we are generally responsible for expenses related to the development of the AffaMed Licensed Products in the applicable Fields in the Territories, provided that AffaMed (i) reimburse us a low-teen percentage of expenses incurred in connection with certain clinical trials conducted by us and designed to support marketing approval of the AffaMed Licensed Product by FDA or the European Medicines Agency, or the Global Studies; (ii) is solely responsible for expenses incurred in connection with territory-specific clinical trials that it conducts in furtherance of the development plan agreed between the parties in the applicable Fields in the Territories, or the Local Studies; and (iii) reimburse us in full for expenses incurred in connection with obtaining and maintaining regulatory approvals of the AffaMed Licensed Products in the applicable Fields in the Territories. In the event AffaMed declines to participate in a Global Study or to conduct a Local Study in any jurisdiction in which we determine to conduct such a study, we are relieved of our obligation to provide AffaMed clinical data from such study, other than safety data, unless AffaMed subsequently reimburses us in the amounts described above plus a prespecified premium.

AffaMed is further obligated, at its sole cost and expense, to use commercially reasonable efforts to commercialize the AffaMed Licensed Products in the applicable Fields in the Territories. The AffaMed License Agreement contemplates that the parties negotiate and enter into a future agreement requiring us to use commercially reasonable efforts to manufacture and supply finished drug products in sufficient quantity for clinical development and commercialization of the AffaMed Licensed Products in the applicable Fields in the Territories.

In accordance with its terms, the AffaMed License Agreement expires upon the expiration of the last royalty term for the last AffaMed Licensed Product in any applicable Field in the Territories. Either party may, subject to specified cure periods, terminate the AffaMed License Agreement in the event of the other party's uncured breach. Either party may also terminate the AffaMed License Agreement under specified circumstances relating to the other party's insolvency. During an established period following a change of control of us or our entry into a global licensing agreement that includes the Territories with a third party, we have the option to terminate the AffaMed License Agreement, subject to a specified notice period and the repayment of any costs and expenses incurred by AffaMed in connection with the AffaMed License Agreement, including upfront and milestone payments AffaMed has previously paid to us, at a prespecified premium. AffaMed has the right to terminate the AffaMed License Agreement at any time following the completion of a Phase 3 clinical trial to evaluate PAXTRAVA.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technologies, knowledge, experience and scientific resources provide us with competitive advantages, potential competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical and generic drug companies, and compounding pharmacies. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Many of our potential competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

The key competitive factors affecting the success of each of our product candidates, if approved for marketing, are likely to be efficacy, safety, method and frequency of administration, convenience, price, the level of generic competition and the availability of coverage and adequate reimbursement from government and other third-party payors.

Because the active pharmaceutical ingredients in our product candidates are available on a generic basis, or are soon to be available on a generic basis, competitors will be able to offer and sell products with the same active pharmaceutical ingredient as our products so long as these competitors do not infringe the patents that we license. For example, our licensed patents related to our intracanalicular insert product candidates largely relate to the hydrogel composition of the intracanalicular inserts and certain drug-release features of the intracanalicular inserts. As such, if a third party were able to design around the formulation and process patents that we license and create a different formulation using a different production process not covered by our licensed patents or patent applications, we would likely be unable to prevent that third party from manufacturing and marketing its product.

Competitors of AXPAXLI

Our intravitreal implant for the treatment of wet AMD will compete with anti-VEGF compounds administered in their current formulation and prescribed for the treatment of wet AMD as these agents can in some instances deliver three to four months or more of therapeutic effect. They include Lucentis, Eylea and Eylea HD, Beovu, Vabysmo and off-label use of the cancer therapy Avastin. Multiple companies, although all in early stages of development, are exploring ways to deliver anti-VEGF products in a sustained-release fashion, including Regeneron which received approval for its 8mg version of Eylea in August 2023; Clearside Biomedical, which is pursuing a TKI (axitinib) administered into the suprachoroidal space; Eyepoint Pharmaceuticals, which is pursuing a sustained-release bioerodible device containing a TKI (vorolanib) using its Durasert technology; Aerie Pharmaceuticals, which is pursuing development of a four to six month TKI implant (axitinib) using its Print® manufacturing technology; and Kodiak Sciences, which is pursuing sustained release therapies based on its anti-VEGF biopolymer conjugate technology. In October 2021, Genentech received approval for Susvimo which utilizes the company's port delivery system for delivery of ranibizumab but has recently launched a voluntary recall of the product due to manufacturing issues. In addition, there are several companies pursuing gene therapy to treat retinal diseases including Adverum Biotechnologies, and REGENXBIO. There also are a number of companies with products in development targeting the inhibition of the complement system to address retinal diseases, specifically geographic atrophy, or GA, including Apellis Pharmaceuticals, IVERIC bio, now owned by Astellas Pharma, Annexion Biosciences, Novartis (Gyroscope Therapeutics), Genentech/Ionis and Janssen Pharmaceuticals, among others. Apellis received approval of SYFOVRE as the first approved treatment for GA in February 2023, and IVERIC bio's Izervay was approved for the treatment of GA in August 2023.

Competitors of PAXTRAVA

Allergan, now owned by AbbVie, received approval in March 2020 of DURYSTA, a biodegradable bimatoprost intracameral implant consisting of a PGA and a biodegradable polymer matrix for the reduction of IOP in patients with OAG or OHT. Allergan purchased ForSight VISION5 who was conducting a Phase 2 clinical trial with the Helios insert, a sustained-release ocular insert placed below the eyelid that delivers bimatoprost for the treatment of glaucoma. In December 2023, Glaukos received approval for iDose, a prostaglandin analog indicated for the reduction of IOP in patients with OHT or OAG. In addition, several other companies have announced their intention to develop products for treatment of glaucoma using sustained-release therapy, although each of these is at an early stage of development. Mati Therapeutics has conducted a Phase 2 clinical trial with an intracanalicular insert for the treatment of glaucoma.

Competitors of OTX-DED and OTX-CSI

A number of therapies are currently available for the treatment of dry eye disease in the United States. The most commonly used treatments for dry eye disease in the United States are over-the-counter eye drops, often referred to as "artificial tears," and there are three FDA-approved prescription eye drop therapies: Restasis, Xiidra and Cequa. Artificial tears are intended to supplement insufficient tear production or improve tear film instability but are primarily saline-based and provide only temporary relief. Restasis and Cequa, both calcineurin inhibitor immunosuppressants, and Xiidra, a LFA-1 antagonist, address chronic inflammation associated with dry eye disease. Kala Pharmaceuticals received approval in 2020 and launched EYSUVIS, (loteprednol etabonate ophthalmic suspension) 0.25% for the short term (up to two weeks) treatment of the signs and symptoms of dry eye disease. EYSUVIS was sold to Alcon in July 2022. Oyster Point Pharma received approval in 2021 for TYRVAYA (varenicline solution) Nasal Spray, a cholinergic agonist indicated for the treatment of the signs and symptoms of dry eye disease. Oyster Point was purchased by Viatris in November 2022. Other treatment options include ointments, gels, warm compresses, omega-3 fatty acid supplements and a number of medical devices. We are aware of many other companies developing therapies for dry eye disease, including Aerie Pharmaceuticals, Alcon, Aldeyra Therapeutics, Allergan, Aurinia Pharmaceuticals, Azura Ophthalmics, Bausch Health (Novaliq), HanAll BioPharma, Johnson & Johnson, Mitotech, Novartis, Parion Sciences, ReGenTree, Silk Technologies, Sylentis, TearSolutions, and TopiVert Pharma.

Competitors of DEXTENZA

Icon Biosciences, Inc. received FDA approval of DEXYCU in February 2018. DEXYCU is an injection of dexamethasone at the time of surgery into the posterior chamber of the eye (behind the iris) to treat inflammation associated with cataract surgery. Icon Biosciences Inc. was subsequently bought by pSvidia Corporation in March 2018 and, at the same time, the new entity was renamed Eyepoint. Eyepoint launched DEXYCU commercially in the first quarter of 2019. DEXYCU lost separate government reimbursement as of January 1, 2023 and is no longer actively marketed. OMIDRIA, purchased by Rayner Surgical Group Limited, is a prescription medication used during cataract surgery. According to the OMIDRIA website, this product helps the black part in the center of your eye (pupil) stay open (dilated) during cataract surgery and decreases eye pain after surgery.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, clearance, approval, pricing, sales, reimbursement, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products and medical devices. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Review and Approval of Drugs and Biologics in the United States

In the United States, the FDA approves and regulates drugs under the FDCA and related regulations. Drugs are also subject to other federal, state and local statutes and regulations. Biological products are licensed for marketing under the Public Health Service Act, or PHSA, and subject to regulation under the FDCA and related regulations, and other federal, state and local statutes and regulations. A company, institution, or organization which takes responsibility for the initiation and management of a clinical development program for such products is referred to as a sponsor. A sponsor seeking approval to market and distribute a new drug or biological product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA’s good laboratory practice, or GLP, regulations;

- design of a clinical protocol and submission to the FDA of an IND, which must take effect before human clinical trials may begin;

- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;

- performance of adequate and well-controlled human clinical trials in accordance with GCPs, to establish the safety and efficacy of the proposed drug product for each indication;

- preparation and submission to the FDA of a new drug application, or NDA, demonstrating the safety and efficacy for the drug candidate product or, with respect to biologics, a biological licensing application, or

BLA, demonstrating the safety, purity and potency of the proposed biological product for one or more proposed indications;

- review by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of clinical data;
- payment of user fees and securing FDA approval of the NDA or BLA; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

Preclinical Studies

Preclinical studies include laboratory evaluation of the purity and stability of the manufactured drug substance or active pharmaceutical ingredient and the formulated product, as well as *in vitro* and animal studies to assess the safety and activity of the investigational product for initial testing in humans and to establish a rationale for therapeutic use. These studies are generally referred to as IND-enabling studies. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations and standards and the United States Department of Agriculture's Animal Welfare Act. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, are submitted to the FDA as part of an IND.

Companies usually must complete some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and must also develop additional information about the chemistry and physical characteristics of the investigational product and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the candidate product and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the candidate product does not undergo unacceptable deterioration over its shelf life.

The IND and IRB Processes

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their voluntary informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug or biologic that is not the subject of an approved NDA or BLA. In support of a request for an IND, sponsors must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to assure the safety and rights of patients and to help assure that the quality of the investigation will be adequate to permit an evaluation of the drug's effectiveness and safety and of the biological product's safety, purity and potency. At any time during this 30-day period, or thereafter, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

The FDA's primary objectives in reviewing an IND are to assure the safety and rights of patients and to help assure that the quality of the investigation will be adequate to permit an evaluation of the drug's effectiveness and safety and of the biological product's safety, purity and potency. The decision to terminate development of an investigational drug or biological product may be made by either a health authority body such as the FDA, an IRB or ethics committee, or by us for various reasons. Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board, or DSMB, or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk.

Reporting Clinical Trial Results

Under the PHSA, sponsors of clinical trials of certain FDA-regulated products, including prescription drugs and biologics, are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the U.S. National Institutes of Health, or NIH. In particular, information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Although sponsors are also obligated to disclose the results of their clinical trials after completion, disclosure of the results can be delayed in some cases for up to two years after the date of completion of the trial. The NIH's Final Rule on registration and reporting requirements for clinical trials became effective in 2017.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

There is no obligation for a sponsor to make its investigational products available for expanded access; however, as required by amendments to the FDCA included in the 21st Century Cures Act, or the Cures Act, passed in 2016, if a sponsor has a policy regarding how it responds to expanded access requests with respect to product candidates in development to treat serious diseases or conditions, it must make that policy publicly available. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study for a covered investigational product; or 15 days after the investigational product receives designation from the FDA as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

In addition, on May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Human Clinical Studies in Support of an NDA or BLA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

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

- Phase 1: The drug or biologic is initially introduced into a small number of healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.

- Phase 2: The drug or biologic is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- Phase 3: The drug or biologic is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

In some cases, the FDA may approve an NDA or BLA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate's safety and effectiveness after approval. Such post-approval trials, typically referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of a larger number of patients in the intended treatment group. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials, such as to verify clinical benefit in the case of products approved under accelerated approval regulations. Failure to exhibit due diligence with regard to conducting mandatory Phase 4 clinical trials could result in withdrawal of FDA approval for products.

A clinical trial may combine the elements of more than one phase, and the FDA often requires more than one Phase 3 trial to support marketing approval of a product candidate. A company's designation of a clinical trial as being of a particular phase is not necessarily indicative that the study will be sufficient to satisfy the FDA requirements of that phase because this determination cannot be made until the protocol and data have been submitted to and reviewed by the FDA. Moreover, as noted above, a pivotal trial is a clinical trial that is believed to satisfy FDA requirements for the evaluation of a product candidate's safety and efficacy such that it can be used, alone or with other pivotal or non-pivotal trials, to support regulatory approval. Generally, pivotal trials are Phase 3 trials, but they may be Phase 2 trials if the design provides a well-controlled and reliable assessment of clinical benefit, particularly in an area of unmet medical need.

In December 2022, with the passage of Food and Drug Omnibus Reform Act, or FDORA, Congress began requiring sponsors to develop and submit a diversity action plan for each Phase 3 clinical trial or any other “pivotal study” of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, actions plans must include the sponsor’s goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In addition to these requirements, the legislation directs the FDA to issue new guidance on diversity action plans.

In June 2023, the FDA issued draft guidance with updated recommendations for GCPs aimed at modernizing the design and conduct of clinical trials. The updates are intended to help pave the way for more efficient clinical trials to facilitate the development of medical products. The draft guidance is adopted from the International Council for Harmonisation’s recently updated E6(R3) draft guideline that was developed to enable the incorporation of rapidly developing technological and methodological innovations into the clinical trial enterprise. In addition, the FDA issued draft guidance outlining recommendations for the implementation of decentralized clinical trials.

Clinical Trials Outside the United States in Support of FDA Approval

We generally plan to conduct our later stage and pivotal clinical trials of our product candidates in the United States. Nonetheless, in connection with our clinical development program, we may have trial sites outside the United States. When a foreign clinical trial is conducted under an IND, all IND requirements must be met unless waived. When a foreign clinical trial is not conducted under an IND, the sponsor must ensure that the trial complies with certain regulatory requirements of the FDA in order to use the trial as support for an IND or application for marketing approval. Specifically, the trials must be conducted in accordance with GCP, including undergoing review and receiving approval by an independent ethics committee, or IEC, and seeking and receiving informed consent from subjects. GCP requirements encompass both ethical and data integrity standards for clinical studies. The FDA’s regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical trials, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign trials are conducted in a manner comparable to that required for IND trials.

The acceptance by the FDA of trial data from clinical trials conducted outside the United States in support of US approval may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

In addition, even where the foreign trial data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the trial is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the trial through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials are subject to the applicable local laws of the foreign jurisdictions where the trials are conducted.

Interactions with FDA During the Clinical Development Program

Following the clearance of an IND and the commencement of clinical trials, the sponsor will continue to have interactions with the FDA. Progress reports detailing the results of clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the product candidate; and any clinically important increase in the occurrence of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

In addition, sponsors are given opportunities to meet with the FDA at certain points in the clinical development program. Specifically, sponsors may meet with the FDA prior to the submission of an IND (pre-IND meeting), at the end of Phase 2 clinical trial (EOP2 meeting) and before an NDA or BLA is submitted (pre-NDA or pre-BLA meeting). Meetings at other times may also be requested. There are five types of meetings that occur between sponsors and the FDA. Type A meetings are those that are necessary for an otherwise stalled product development program to proceed or to address an important safety issue. Type B meetings include pre-IND and pre-NDA/pre-BLA meetings, as well as end of phase meetings such as EOP2 meetings. A Type C meeting is any meeting other than a Type A or Type B meeting regarding the development and review of a product, including for example meetings to facilitate early consultations on the use of a biomarker as a new surrogate endpoint that has never been previously used as the primary basis for product approval in the proposed context of use. A Type D meeting is focused on a narrow set of issues, which should be limited to no more than two focused topics and should not require input from more than three disciplines or Divisions. Finally, INTERACT meetings are intended for novel products and development programs that present unique challenges in the early development of an investigational product.

These meetings provide an opportunity for the sponsor to share information about the data gathered to date with the FDA and for the FDA to provide advice on the next phase of development. For example, at an EOP2 meeting, a sponsor may discuss its Phase 2 clinical results and present its plans for the pivotal Phase 3 clinical trial(s) that it believes will support the approval of the new product. Such meetings may be conducted in person, via teleconference/videoconference or written response only with minutes reflecting the questions that the sponsor posed to the FDA and the FDA's responses. The FDA has indicated that its responses, as conveyed in meeting minutes and advice letters, only constitute mere recommendations and/or advice made to a sponsor and, as such, sponsors are not bound by such recommendations and/or advice. From a practical perspective, a sponsor's failure to follow the FDA's recommendations for design of a clinical program may put the program at significant risk of failure.

Special Protocol Assessment Agreements

A Special Protocol Assessment, or SPA, agreement is an agreement between a sponsor and the FDA on the design and size of studies and clinical trials that can be used for approval of a drug or biological product. The FDA's guidance on such agreements states that an agreement may not be changed by the sponsor or the agency unless through a written agreement of the two entities or if FDA determines there is a substantial scientific issue essential to determining the safety or effectiveness of the drug or the safety, potency or purity of the biologic product. The protocols that are eligible for SPA agreements are: animal carcinogenicity protocols, final product stability protocols and clinical protocols for Phase 3 trials where the data will form the primary basis for an efficacy claim.

The FDA may meet with sponsors, provided certain conditions are met, for the purpose of reaching an SPA agreement on the design and size of clinical trials intended to form the primary basis of an efficacy claim in a marketing application. If a sponsor makes a reasonable written request to meet with the FDA for the purpose of reaching agreement on the design and size of a clinical trial, then the FDA will meet with the sponsor. If an agreement is reached, the FDA will reduce the agreement to writing and make it part of the administrative record. An agreement may not be changed by the sponsor or FDA after the trial begins, except with the written agreement of the sponsor and FDA, or if the director of the FDA reviewing division determines that "a substantial scientific issue essential to determining the safety or effectiveness of the investigational product was identified after the testing began. If a sponsor and the FDA meet regarding the design and size of a clinical trial and the parties cannot agree that the trial design is adequate to meet the goals of the sponsor, the FDA will clearly state the reasons for the disagreement in a letter to the sponsor.

Manufacturing and Other Regulatory Requirements

Concurrently with clinical trials, sponsors usually complete additional animal safety studies, develop additional information about the chemistry and physical characteristics of the product candidate and finalize a process for manufacturing commercial quantities of the product candidate in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other criteria, the sponsor must develop methods for testing the identity, strength, quality, and purity of the finished product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Specifically, the FDA's regulations require that pharmaceutical products be manufactured in specific approved facilities and in accordance with cGMPs. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports and returned or salvaged products. Manufacturers and other entities involved in the manufacture and distribution of approved pharmaceuticals are required to register their establishments with the FDA and some state agencies, and they are subject to periodic unannounced inspections by the FDA for compliance with cGMPs and other requirements. Inspections must follow a "risk-based schedule" that may result in certain establishments being inspected more frequently. Manufacturers may also have to provide, on request, electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA may lead to a product being deemed to be adulterated. Changes to the manufacturing process, specifications or container closure system for an approved product are strictly regulated and often require prior FDA approval before being implemented. The FDA's regulations also require, among other things, the investigation and correction of any deviations from cGMP and the imposition of reporting and documentation requirements upon the sponsor and any third-party manufacturers involved in producing the approved product.

The PREVENT Pandemics Act, which was enacted in December 2022, clarifies that foreign drug manufacturing establishments are subject to registration and listing requirements even if a drug or biologic undergoes further manufacture, preparation, propagation, compounding, or processing at a separate establishment outside the United States prior to being imported or offered for import into the United States.

Pediatric Studies

Under the Pediatric Research Equity Act, or PREA, applications and certain types of supplements to applications must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor must submit an initial Pediatric Study Plan, or PSP, within 60 days of an EOP2 meeting or as may be agreed between the sponsor and the FDA. Those plans must contain an outline of the proposed pediatric study or studies the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The sponsor and the FDA must reach agreement on a final plan. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical studies, early phase clinical trials, and/or other clinical development programs.

The FDA may, on its own initiative or at the request of the sponsor, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. Pursuant to the Food and Drug Administration Safety and Innovation Act of 2012, or FDASIA, the FDA must send a PREA Non-Compliance letter to sponsors who have failed to submit their pediatric assessments required under PREA, have failed to seek or obtain a deferral or deferral extension or have failed to request approval for a required pediatric formulation. It further requires the FDA to publicly post the PREA Non-Compliance letter and sponsor's response. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation, although the FDA has recently taken steps to limit what it considers abuse of this statutory exemption in PREA by announcing that it does not intend to grant any additional orphan drug designations for rare pediatric subpopulations of what is otherwise a common disease. The FDA also maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population. In May 2023, the FDA issued new draft guidance that further describes the pediatric study requirements under PREA.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical studies which must contain substantial evidence of the safety and efficacy of the proposed new product. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the sponsor to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the sponsor for approval of the application "were not conducted by or for the sponsor and for which the sponsor has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Section 505(b)(2) thus authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the sponsor. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) sponsor can establish that reliance on the FDA's previous approval is scientifically appropriate, the sponsor may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) sponsor.

If we obtain favorable results in our clinical trials, we plan to submit NDAs for our product candidates under Section 505(b)(2).

Acceptance and Review of NDAs and BLAs

Assuming successful completion of the required clinical testing, the results of the preclinical studies and clinical trials, along with information relating to the product's chemistry, manufacturing, controls, safety updates, patent information, abuse information and proposed labeling, are submitted to the FDA as part of an application requesting approval to market the product candidate for one or more indications. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of a drug product and the safety, potency and purity of the biological product to the satisfaction of the FDA. The fee required for the submission and review of an application under the Prescription Drug User Fee Act, or PDUFA, is substantial (for example, for FY2024 this application fee is approximately $4.0 million), and the sponsor of an approved application is also subject to an annual program fee, which for FY2024 is currently set at $416,734 per eligible prescription product. These fees are typically adjusted annually, and exemptions and waivers may be available under certain circumstances, such as where a waiver is necessary to protect the public health, where the fee would present a significant barrier to innovation, or where the sponsor is a small business submitting its first human therapeutic application for review.

The FDA conducts a preliminary review of all applications within 60 days of receipt and must inform the sponsor at that time or before whether an application is sufficiently complete to permit substantive review. In pertinent part, FDA's regulations state that an application "shall not be considered as filed until all pertinent information and data have been received" by the FDA. In the event that FDA determines that an application does not satisfy this standard, it will issue a Refuse to File, or RTF, determination to the sponsor. Typically, an RTF will be based on administrative incompleteness, such as clear omission of information or sections of required information; scientific incompleteness, such as omission of critical data, information or analyses needed to evaluate safety and efficacy or provide adequate directions for use; or inadequate content, presentation, or organization of information such that substantive and meaningful review is precluded. The FDA may request additional information rather than accept an application for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing.

After the submission is accepted for filing, the FDA begins an in-depth substantive review of the application. The FDA reviews the application to determine, among other things, whether the proposed product is safe and effective for its intended use, whether it has an acceptable purity profile and whether the product is being manufactured in accordance with cGMP. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has ten months from the filing date in which to complete its initial review of a standard application that is a new molecular entity, and six months from the filing date for an application with "priority review." The review process may be extended by the FDA for three additional months to consider new information or in the case of a clarification provided by the sponsor to address an outstanding deficiency identified by the FDA following the original submission. Despite these review goals, it is not uncommon for FDA review of an application to extend beyond the PDUFA target action date.

In connection with its review of an application, the FDA will typically submit information requests to the sponsor and set deadlines for responses thereto. The FDA will also conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether the manufacturing processes and facilities comply with cGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and are adequate to assure consistent production of the product within required specifications.

The FDA also may inspect the sponsor and one or more clinical trial sites to assure compliance with IND and GCP requirements and the integrity of the clinical data submitted to the FDA. With passage of FDORA, Congress clarified FDA's authority to conduct inspections by expressly permitting inspection of facilities involved in the preparation, conduct, or analysis of clinical and non-clinical studies submitted to FDA as well as other persons holding study records or involved in the study process. To ensure cGMP and GCP compliance by its employees and third-party contractors, a sponsor may incur significant expenditure of time, money and effort in the areas of training, record keeping, production and quality control.

Additionally, the FDA may refer an application, including applications for novel product candidates which present difficult questions of safety or efficacy, to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it considers such recommendations when making final decisions on approval. Data from clinical trials are not always conclusive, and the FDA or its advisory committee may interpret data differently than the sponsor interprets the same data. The FDA may also re-analyze the clinical trial data, which could result in extensive discussions between the FDA and the sponsor during the review process.

The FDA also may require submission of a Risk Evaluation and Mitigation Strategy, or REMS, if it determines that a REMS is necessary to ensure that the benefits of the product outweigh its risks and to assure the safe use of the product. The REMS could include medication guides, physician communication plans, assessment plans and/or elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools. The FDA determines the requirement for a REMS, as well as the specific REMS provisions, on a case-by-case basis. If the FDA concludes a REMS is needed, the sponsor of the application must submit a proposed REMS and the FDA will not approve the application without a REMS.

Decisions on NDAs and BLAs

The FDA reviews a sponsor to determine, among other things, whether the product is safe and whether it is effective for its intended use(s), with the latter determination being made on the basis of substantial evidence. The term "substantial evidence" is defined under the FDCA as "evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the product involved, on the basis of which it could fairly and responsibly be concluded by such experts that the product will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof."

The FDA has interpreted this evidentiary standard to require at least two adequate and well-controlled clinical investigations to establish effectiveness of a new product. Under certain circumstances, however, FDA has indicated that a single trial with certain characteristics and additional information may satisfy this standard. This approach was subsequently endorsed by Congress in 1998 with legislation providing, in pertinent part, that "If FDA determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, FDA may consider such data and evidence to constitute substantial evidence." This modification to the law recognized the potential for FDA to find that one adequate and well controlled clinical investigation with confirmatory evidence, including supportive data outside of a controlled trial, is sufficient to establish effectiveness. In December 2019, FDA issued draft guidance further explaining the studies that are needed to establish substantial evidence of effectiveness. The FDA has not yet finalized that guidance.

After evaluating the application and all related information, including the advisory committee recommendations, if any, and inspection reports of manufacturing facilities and clinical trial sites, the FDA will issue either a CRL or an approval letter. To reach this determination, the FDA must determine that the drug is effective and that its expected benefits outweigh its potential risks to patients. This "benefit-risk" assessment is informed by the extensive body of evidence about the product's safety and efficacy in the NDA or BLA. This assessment is also informed by other factors, including: the severity of the underlying condition and how well patients' medical needs are addressed by currently available therapies; uncertainty about how the premarket clinical trial evidence will extrapolate to real-world use of the product in the post-market setting; and whether risk management tools are necessary to manage specific risks. In connection with this assessment, the FDA review team will assemble all individual reviews and other documents into an "action package," which becomes the record for FDA review. The review team then issues a recommendation, and a senior FDA official makes a decision.

A CRL indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A CRL generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. The CRL may require additional clinical or other data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time- consuming requirements related to clinical trials, preclinical studies or manufacturing. If a CRL is issued, the sponsor will have one year to respond to the deficiencies identified by the FDA, at which time the FDA can deem the application withdrawn or, in its discretion, grant the sponsor an additional six-month extension to respond. The FDA has committed to reviewing resubmissions in response to an issued CRL in either two or six months depending on the type of information included. Even with the submission of this additional information, however, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. The FDA has taken the position that a CRL is not final agency action making the determination subject to judicial review. For those seeking to challenge FDA's CRL decision, the FDA has indicated that sponsors may request a formal hearing on the CRL or file a request for reconsideration or a request for a formal dispute resolution.

An approval letter, on the other hand, authorizes commercial marketing of the product with specific prescribing information for specific indications. That is, the approval will be limited to the conditions of use (e.g., patient population, indication) described in the FDA-approved labeling. Further, depending on the specific risk(s) to be addressed, the FDA may require that contraindications, warnings or precautions be included in the product labeling, require that post-approval trials, including Phase 4 clinical trials, be conducted to further assess a product's safety after approval, require testing and surveillance programs to monitor the product after commercialization or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing trials or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Under the Ensuring Innovation Act, which was signed into law in April 2021, the FDA must publish action packages summarizing its decisions to approve new drugs and biologics within 30 days of approval of such products. To date, CRLs are not publicly available documents.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a drug.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

With passage of FDORA, Congress modified certain provisions governing accelerated approval of drug and biologic products. Specifically, the new legislation authorized the FDA to: require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded, require a sponsor of a product granted accelerated approval to submit progress reports on its post-approval studies to FDA every six months until the study is completed; and use expedited procedures to withdraw accelerated approval of an NDA or BLA after the confirmatory trial fails to verify the product's clinical benefit. Further, FDORA requires the FDA to publish on its website "the rationale for why a post-approval study is not appropriate or necessary" whenever it decides not to require such a study upon granting accelerated approval.

In March 2023, the FDA issued draft guidance that outlines its current thinking and approach to accelerated approval. The guidance provides that although single-arm trials have been commonly used to support accelerated approval, a randomized controlled trial is the preferred approach as it provides a more robust efficacy and safety assessment and allows for direct comparisons to an available therapy. While this guidance is currently only in draft form and will ultimately not be legally binding even when finalized, sponsors typically observe FDA's guidance closely to ensure that their investigational products qualify for accelerated approval.

Post-Approval Regulation

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

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

A product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release, the manufacturer must submit samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot, to the FDA. The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency and effectiveness of pharmaceutical products.

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

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

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the HHS, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug or biologic.

It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information. Moreover, with passage of the Pre-Approval Information Exchange Act, or PIE Act, in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products and product candidates in development to help expedite patient access upon product approval. Previously, such communications were permitted under FDA guidance but the new legislation explicitly provides protection to sponsors who convey certain information about products and product candidates in development to payors, including unapproved uses of approved products. In addition, in October 2023, the FDA published draft guidance outlining the agency's non-binding policies governing the distribution of scientific information on unapproved uses to healthcare providers. This draft guidance calls for such communications to be truthful, non-misleading, factual, and unbiased and include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use.

In addition, the distribution of prescription pharmaceutical products is subject to a variety of federal and state laws, the most recent of which is still in the process of being phased into the U.S. supply chain and regulatory framework. The Prescription Drug Marketing Act, or PDMA, was the first federal law to set minimum standards for the registration and regulation of drug distributors by the states and to regulate the distribution of drug samples. Today, both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. Congress more recently enacted the Drug Supply Chain Security Act, or DSCSA, which made significant amendments to the FDCA, including by replacing certain provisions from the PDMA pertaining to wholesale distribution of prescription drugs with a more comprehensive statutory scheme. The DSCSA now requires uniform national standards for wholesale distribution and, for the first time, for third-party logistics providers; it also provides for preemption of certain state laws in the areas of licensure and prescription drug traceability.

Generic Drugs and Regulatory Exclusivity

In 1984, with passage of the Hatch-Waxman Act, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs and it also enacted Section 505(b)(2). To obtain approval of a generic drug, a sponsor must submit an abbreviated new drug application, or ANDA, to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing conducted for a drug product previously approved under an NDA, known as the reference listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, the strength of the drug and the conditions of use of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug." Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD.

Under the Hatch-Waxman Act, the FDA may not approve an ANDA or 505(b)(2) application until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity, or NCE. For the purposes of this provision, FDA has consistently taken the position that an NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. This interpretation was confirmed with enactment of the Ensuring Innovation Act in April 2021. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, a generic or follow-on drug application may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the sponsor may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the sponsor and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as new indications, dosage forms, route of administration or combination of ingredients. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs or 505(b)(2) NDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product; rather, this three-year exclusivity covers only the conditions of use associated with the new clinical investigations and, as a general matter, does not prohibit the FDA from approving follow-on applications for drugs containing the original active ingredient.

Five-year and three-year exclusivity also will not delay the submission or approval of a traditional NDA filed under Section 505(b)(1) of the FDCA; however, a sponsor submitting a traditional NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

As part of the submission of an NDA or certain supplemental applications, NDA sponsors are required to list with the FDA each patent with claims that cover the sponsor's product or an approved method of using the product. Upon approval of a new drug, each of the patents listed in the application for the drug is then published in the Orange Book. The FDA's regulations governing patient listings were largely codified into law with enactment of the Orange Book Modernization Act in January 2021. When an ANDA sponsor files its application with the FDA, the sponsor is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book. Specifically, the ANDA sponsor must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. Moreover, to the extent that the Section 505(b)(2) NDA sponsor is relying on studies conducted for an already approved product, the sponsor also is required to certify to the FDA concerning any patents listed for the NDA-approved product in the Orange Book to the same extent that an ANDA sponsor would.

If the generic drug or follow-on drug sponsor does not challenge the innovator's listed patents, FDA will not approve the ANDA or 505(b)(2) application until all the listed patents claiming the referenced product have expired. A certification that the new generic product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the ANDA sponsor has provided a Paragraph IV certification to the FDA, the sponsor must also send notice of the Paragraph IV certification to the NDA owner and patent holders once the ANDA has been accepted for filing by the FDA. The NDA owner and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the

FDA from approving the ANDA or 505(b)(2) NDA until the earliest of 30 months after the receipt of the Paragraph IV notice, expiration of the patent and a decision in the infringement case that is favorable to the ANDA or 505(b)(2) NDA sponsor.

Regulatory Exclusivity Governing Biologics

When a biological product is licensed for marketing by FDA with approval of a BLA, the product may be entitled to certain types of market and data exclusivity barring FDA from approving competing products for certain periods of time. In March 2010, the Patient Protection and Affordable Care Act was enacted in the United States and included the Biologics Price Competition and Innovation Act of 2009, or the BPCIA. The BPCIA amended the PHSA to create an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Since enactment of this statute, the FDA has approved a number of biosimilars and interchangeable biosimilar products.

Under the BPCIA, a manufacturer may submit an application for a product that is "biosimilar to" a previously approved biological product, which the statute refers to as a "reference product." In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and the proposed biosimilar product in terms of safety, purity and potency. The biosimilar sponsor may demonstrate that its product is biosimilar to the reference product on the basis of data from analytical studies, animal studies and one or more clinical studies to demonstrate safety, purity and potency in one or more appropriate conditions of use for which the reference product is approved. In addition, the sponsor must show that the biosimilar and reference products have the same mechanism of action for the conditions of use on the label, route of administration, dosage and strength, and the production facility must meet standards designed to assure product safety, purity and potency.

For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find not only that the product is biosimilar to the reference product but also that it can be expected to produce the same clinical results as the reference product such that the two products may be switched without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. Upon licensure by the FDA, an interchangeable biosimilar may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product. Following approval of the interchangeable biosimilar product, the FDA may not grant interchangeability status for any second biosimilar until one year after the first commercial marketing of the first interchangeable biosimilar product. In December 2022, Congress clarified through FDORA that FDA may approve multiple first interchangeable biosimilar biological products so long as the products are all approved on the first day on which such a product is approved as interchangeable with the reference product.

A reference biological product is granted 12 years of exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. Even if a product is considered to be a reference product eligible for exclusivity, however, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the sponsor's own preclinical data and data from adequate and well controlled clinical trials to demonstrate the safety, purity, and potency of their product. There have been recent government proposals to reduce the 12-year reference product exclusivity period, but none has been enacted to date. At the same time, since passage of the BPCIA, many states have passed laws or amendments to laws, which address pharmacy practices involving biosimilar products.

Pediatric Exclusivity

Pediatric exclusivity is a type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of exclusivity. For drug products, the six-month exclusivity may be attached to the term of any existing patent or regulatory exclusivity, including the orphan exclusivity and regulatory exclusivities available under the Hatch-Waxman Act. For biologic products, the six-month period may be attached to any existing regulatory exclusivities but not to any patent terms. The conditions for pediatric exclusivity include the FDA's determination that information relating to the use of a new product in the pediatric population may produce health benefits in that population, the FDA making a written request for pediatric clinical trials, and the sponsor agreeing to perform, and reporting on, the requested clinical trials within the statutory timeframe. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patents that cover the product are extended by six months. Although this is not a patent term extension, it effectively extends the regulatory period during which the FDA cannot approve another application. With regard to patents, the six-month pediatric exclusivity period will not attach to any patents for which an ANDA or 505(b)(2) sponsor submitted a paragraph IV patent certification, unless the NDA sponsor or patent owner first obtains a court determination that the patent is valid and infringed by the proposed product.

Patent Term Restoration and Extension

In the United States, a patent claiming a new product, its method of use or its method of manufacture may be eligible for a limited patent term extension under the Hatch Waxman Act, which permits a patent extension of up to five years for patent term lost during product development and FDA regulatory review. Assuming grant of the patent for which the extension is sought, the restoration period for a patent covering a product is typically one half the time between the effective date of the IND involving human beings and the submission date of the NDA or BLA, plus the time between the submission date of the application and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date in the United States. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent for which extension is sought. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension in consultation with the FDA.

Review and Approval of Medical Devices in the United States

Medical devices in the United States are strictly regulated by the FDA. Under the FDCA, a medical device is defined as an instrument, apparatus, implement, machine, contrivance, implant, *in vitro* reagent, or other similar or related article, including a component part, or accessory which is, among other things: intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals; or intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes. This definition provides a clear distinction between a medical device and other FDA regulated products such as drugs. If the primary intended use of the product is achieved through chemical action or by being metabolized by the body, the product is usually a drug. If not, it is generally a medical device.

Unless an exemption applies, a new medical device may not be marketed in the United States unless and until it has been cleared through filing of a 510(k) premarket notification, or 510(k), or approved by the FDA pursuant to a PMA application. The information that must be submitted to the FDA in order to obtain clearance or approval to market a new medical device varies depending on how the medical device is classified by the FDA. Medical devices are classified into one of three classes on the basis of the controls deemed by the FDA to be necessary to reasonably ensure their safety and effectiveness.

Class I devices are low-risk devices for which reasonable assurance of safety and effectiveness can be provided by adherence to the FDA's general controls for medical devices, which include applicable portions of the FDA's Quality System Regulation, or QSR, facility registration and product listing, reporting of adverse medical events and malfunctions and appropriate, truthful and non-misleading labeling, advertising and promotional materials. Many Class I devices are exempt from premarket regulation; however, some Class I devices require premarket clearance by the FDA through the 510(k) premarket notification process.

Class II devices are moderate-risk devices and are subject to the FDA's general controls, and any other special controls, such as performance standards, post-market surveillance, and FDA guidelines, deemed necessary by the FDA to provide reasonable assurance of the devices' safety and effectiveness. Premarket review and clearance by the FDA for Class II devices are accomplished through the 510(k) premarket notification procedure, although some Class II devices are exempt from the 510(k) requirements. Premarket notifications are subject to user fees, unless a specific exemption applies.

Class III devices are deemed by the FDA to pose the greatest risk, such as those for which reasonable assurance of the device's safety and effectiveness cannot be assured solely by the general controls and special controls described above and that are life-sustaining or life-supporting. A PMA application must provide valid scientific evidence, typically extensive preclinical and clinical trial data and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications (and supplemental PMA applications) are subject to significantly higher user fees than are 510(k) premarket notifications.

510(k) Premarket Notification

To obtain 510(k) clearance, a manufacturer must submit a premarket notification demonstrating that the proposed device is "substantially equivalent" to a predicate device, which is a previously cleared 510(k) device or a pre-amendment device that was in commercial distribution before May 28, 1976, for which the FDA has not yet called for the submission of a PMA application. The FDA's 510(k) clearance pathway usually takes from three to 12 months from the date the application is submitted and filed with the FDA, but it can take significantly longer and clearance is never assured. The FDA has issued guidance documents meant to expedite review of a 510(k) and facilitate interactions between the sponsor and the FDA. To demonstrate substantial equivalence, a manufacturer must show that the device has the same intended use as a predicate device and the same technological characteristics, or the same intended use and different technological characteristics and does not raise new questions of safety and effectiveness than the predicate device.

Most 510(k)s do not require clinical data for clearance, but the FDA may request such data.

The FDA seeks to review and act on a 510(k) within 90 days of submission, but it may take longer if the agency finds that it requires more information to review the 510(k). If the FDA determines that the device is substantially equivalent to a predicate device, the subject device may be marketed. However, if the FDA concludes that a new device is not substantially equivalent to a predicate device, the new device will be classified in Class III and the manufacturer will be required to submit a PMA application to market the product. Devices of a new type that the FDA has not previously classified based on risk are automatically classified into Class III by operation of section 513(f)(1) of the FDCA, regardless of the level of risk they pose. To avoid requiring PMA review of low- to moderate-risk devices classified in Class III by operation of law, Congress enacted section 513(f)(2) of the FDCA. This provision allows the FDA to classify a low- to moderate-risk device not previously classified into Class I or II, a process known as the *de novo* process. A company may apply directly to the FDA for classification of its device as *de novo* or may submit a de novo petition within 30 days of receiving a not substantially equivalent determination.

Modifications to a 510(k)-cleared medical device may require the submission of another 510(k). Modifications to a 510(k)-cleared device frequently require the submission of a traditional 510(k), but modifications meeting certain conditions may be candidates for FDA review under a Special 510(k). If a device modification requires the submission of a 510(k), but the modification does not affect the intended use of the device or alter the fundamental technology of the device, then summary information that results from the design control process associated with the cleared device can serve as the basis for clearing the application. A Special 510(k) allows a manufacturer to declare conformance to design controls without providing new data. When the modification involves a change in material, the nature of the "new" material will determine whether a traditional or Special 510(k) is necessary.

Any modification to a 510(k)-cleared product that would constitute a major change in its intended use or any change that could significantly affect the safety or effectiveness of the device may, in some circumstances, requires the submission of a PMA application, if the change raises complex or novel scientific issues or the product has a new intended use. A manufacturer may be required to submit extensive pre-clinical and clinical data depending on the nature of the changes.

The FDA requires every manufacturer to make the determination regarding the need for a new 510(k) submission in the first instance, but the FDA may review any manufacturer's decision. If the FDA disagrees with the manufacturer's determination and requires new 510(k) clearances or PMA application approvals for modifications to previously cleared products for which the manufacturer concluded that new clearances or approvals are unnecessary, the manufacturer may be required to cease marketing or distribution of the products or to recall the modified product until it obtains clearance or approval, and the manufacturer may be subject to significant regulatory fines or penalties. In addition, the FDA is currently evaluating the 510(k) process and may make substantial changes to industry requirements.

Premarket Approval Application

The PMA application process for approval to market a medical device is more complex, costly, and time- consuming than the 510(k) clearance procedure. A PMA application must be supported by extensive data, including technical information regarding device design and development, preclinical studies, clinical trials, manufacturing and controls information and labeling information that demonstrate the safety and effectiveness of the device for its intended use. After a PMA application is submitted, the FDA has 45 days to determine whether it is sufficiently complete to permit a substantive review. If the PMA application is complete, the FDA will file the PMA application. If the FDA accepts the application for filing, the agency will begin an in-depth substantive review of the application. By statute, the FDA has 180 days to review the application although, generally, review of the application often takes between one and three years, and may take significantly longer. If the FDA has questions, it will likely issue a first major deficiency letter within 150 days of filing. It may also refer the PMA application to an FDA advisory panel for additional review, and will conduct a preapproval inspection of the manufacturing facility to ensure compliance with the QSR, either of which could extend the 180-day response target. In addition, the FDA may request additional information or request the performance of additional clinical trials in which case the PMA application approval may be delayed while the trials are conducted and the data acquired are submitted in an amendment to the PMA. Even with additional trials, the FDA may not approve the PMA application.

If the FDA's evaluations of both the PMA application and the manufacturing facilities are favorable, the FDA will either issue an approval letter authorizing commercial marketing or an approvable letter that usually contains a number of conditions that must be met in order to secure final approval. If the FDA's evaluations are not favorable, the FDA will deny approval of the PMA application or issue a not approvable letter. The PMA application process, including the gathering of clinical and nonclinical data and the submission to and review by the FDA, can take several years, and the process can be expensive and uncertain. Moreover, even if the FDA approves a PMA application, the FDA may approve the device with an indication that is narrower or more limited than originally sought. The FDA can impose post-approval conditions that it believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution. After approval of a PMA application, a new PMA application or PMA application supplement may be required for a modification to the device, its labeling, or its manufacturing process. PMA application supplements often require submission of the same type of information as an initial PMA application, except that the supplement is limited to information needed to support any changes from the device covered by the approved PMA application and may or may not require as extensive technical or clinical data or the convening of an advisory panel. The time for review of a PMA application supplement may vary depending on the type of change, but it can be lengthy. In addition, in some cases the FDA might require additional clinical data.

PMA applications are subject to an application fee. For federal fiscal year 2024, the standard fee is $483,560 and the small business fee is $120,890.

Investigational Device Exemption

A clinical trial is typically required for a PMA application and, in a small percentage of cases, the FDA may require a clinical study in support of a 510(k) submission. A manufacturer that wishes to conduct a clinical study involving the device is subject to the FDA's IDE regulation. The IDE regulation distinguishes between significant and non-significant risk device studies and the procedures for obtaining approval to begin the study differ accordingly. Also, some types of studies are exempt from the IDE regulations. A significant risk device presents a potential for serious risk to the health, safety, or welfare of a subject. Significant risk devices are devices that are substantially important in diagnosing, curing, mitigating, or treating disease or in preventing impairment to human health. Studies of devices that pose a significant risk require both FDA and an IRB approval prior to initiation of a clinical study. Non-significant risk devices are devices that do not pose a significant risk to the human subjects. A non-significant risk device study requires only IRB approval prior to initiation of a clinical study.

An IDE application must be supported by appropriate data, such as animal and laboratory testing results, showing that it is safe to test the device in humans and that the testing protocol is scientifically sound. An IDE application is considered approved 30 days after it has been received by the FDA, unless the FDA otherwise informs the sponsor prior to 30 calendar days from the date of receipt, that the IDE is approved, approved with conditions, or disapproved. The FDA typically grants IDE approval for a specified number of subjects to be enrolled at specified study centers. The clinical trial must be conducted in accordance with applicable regulations, including but not limited to the FDA's IDE regulations and GCP. The investigators must obtain subject informed consent, rigorously follow the investigational plan and study protocol, control the disposition of investigational devices, and comply with all reporting and record keeping requirements. A clinical trial may be suspended or terminated by the FDA, the IRB or the sponsor at any time for various reasons, including a belief that the risks to the study participants outweigh the benefits of participation in the trial. Approval of an IDE does not bind the FDA to accept the results of the trial as sufficient to prove the product's safety and efficacy, even if the trial meets its intended success criteria.

Post-Marketing Restrictions and Enforcement

After a device is placed on the market, numerous regulatory requirements apply. These include but are not limited to:

- submitting and updating establishment registration and device listings with the FDA;
- compliance with the QSR, which require manufacturers to follow stringent design, testing, control, documentation, record maintenance, including maintenance of complaint and related investigation files, and other quality assurance controls during the manufacturing process;
- unannounced routine or for-cause device inspections by the FDA, which may include our suppliers' facilities labeling regulations, which prohibit the promotion of products for uncleared or unapproved or "off-label" uses and impose other restrictions on labeling; and
- post-approval restrictions or conditions, including requirements to conduct post-market surveillance studies to establish continued safety data or tracking products through the chain of distribution to the patient level.

Under the FDA medical device reporting, or MDR, regulations, medical device manufacturers are required to report to the FDA information that a device has or may have caused or contributed to a death or serious injury or has malfunctioned in a way that would likely cause or contribute to death or serious injury if the malfunction of the device or a similar device of such manufacturer were to recur. The decision to file an MDR involves a judgment by the manufacturer. If the FDA disagrees with the manufacturer's determination, the FDA can take enforcement action.

Additionally, the FDA has the authority to require the recall of commercialized products in the event of material deficiencies or defects in design or manufacture. The authority to require a recall must be based on an FDA finding that there is reasonable probability that the device would cause serious injury or death. Manufacturers may, under their own initiative, recall a product if any material deficiency in a device is found. The FDA requires that certain classifications of recalls be reported to the FDA within 10 working days after the recall is initiated.

The failure to comply with applicable regulatory requirements can result in enforcement action by the FDA, which may include any of the following sanctions:

- untitled letters, warning letters, fines, injunctions or civil penalties;
- recalls, detentions or seizures of products;
- operating restrictions;
- delays in the introduction of products into the market;
- total or partial suspension of production;
- delay or refusal of the FDA or other regulators to grant 510(k) clearance or PMA application approvals of new products;
- withdrawals of 510(k) clearance or PMA application approvals; or
- in the most serious cases, criminal prosecution.

To ensure compliance with regulatory requirements, medical device manufacturers are subject to market surveillance and periodic, pre-scheduled and unannounced inspections by the FDA, and these inspections may include the manufacturing facilities of subcontractors.

Review and Approval of Combination Products in the United States

- A combination product is a product composed of any combination of a drug and a device; a biological product and a device; a drug and a biological product; or a drug, device, and a biological product. Under FDA's regulations, a combination product is defined to include: a product comprised of two or more regulated components that are physically, chemically, or otherwise combined or mixed and produced as a single entity (a "single-entity" combination product);

- two or more separate products packaged together in a single package or as a unit and comprised of drug and device products, device and biological products, or biological and drug products ("co-packaged" combination product);

- a drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, device, or biological product (a "cross-labeled" combination product); or

- any investigational drug, device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect (a "cross-labeled" investigational combination product).

The FDA has established an Office of Combination Products to serve as a focal point for combination product issues and for medical product classification and assignment issues for agency staff and industry. That office issues guidance and regulations to clarify the regulation of combination products, and is responsible for assigning products to an FDA center for premarket review and regulation where their classification or assignment is unclear or in dispute. Combination products are assigned to an FDA center based on a determination of the "primary mode of action" or PMOA of the combination product. The FDCA defines PMOA as "the single mode of action of a combination product that provides the most important therapeutic action of the combination product." For example, if the PMOA of a device-biological combination product is attributable to the biological product, the FDA Division responsible for premarket review of that biological product would have primary jurisdiction for the combination product. One investigational application is generally sufficient for a combination product, but that application must include all information on the entire combination product. In most cases, the type of investigational application is that typically required by the lead center. Thus, if the drug constituent part of a drug/device combination product provides the PMOA, the investigation would be under an IND.

Federal and State Data Privacy Laws

There are multiple privacy and data security laws that may impact our business activities, in the United States and in other countries where we conduct trials or where we may do business in the future. These laws are evolving and may increase both our obligations and our regulatory risks in the future. In the health care industry generally, under the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, the HHS has issued regulations to protect the privacy and security of protected health information, or PHI, used or disclosed by covered entities including certain healthcare providers, health plans and healthcare clearinghouses. HIPAA also regulates standardization of data content, codes and formats used in healthcare transactions and standardization of identifiers for health plans and providers. HIPAA also imposes certain obligations on the business associates of covered entities that obtain protected health information in providing services to or on behalf of covered entities. HIPAA may apply to us in certain circumstances and may also apply to our business partners in ways that may impact our relationships with them. Our clinical trials are regulated by the Common Rule, which also includes specific privacy-related provisions. In addition to federal privacy regulations, there are a number of state laws governing confidentiality and security of health information that may be applicable to our business. In addition to possible federal civil and criminal penalties for HIPAA violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state attorneys general (along with private plaintiffs) have brought civil actions seeking injunctions and damages resulting from alleged violations of HIPAA's privacy and security rules. State attorneys general also have authority to enforce state privacy and security laws. New laws and regulations governing privacy and security may be adopted in the future as well.

At the state level, California has enacted legislation that has been dubbed the first "GDPR-like" law in the United States. Known as the California Consumer Privacy Act, or CCPA, it creates new individual privacy rights for consumers (as that word is broadly defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA went into effect on January 1, 2020 and requires covered companies to provide new disclosures to California consumers, provide such consumers new ways to opt-out of certain sales of personal information, and allow for a new cause of action for data breaches. In November 2020, California voters passed a ballot initiative for the California Privacy Rights Act, or the CPRA, which went into effect on January 1, 2023, and significantly expanded the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention, and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created a new enforcement agency – the California Privacy Protection Agency – whose sole responsibility is to enforce the CPRA, which will further increase compliance risk. The provisions in the CPRA may apply to some of our business activities.

In addition to California, at least eleven other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data (which includes health data in some cases). Some of the provisions of these laws may apply to our business activities. There are also states that are strongly considering or have already passed comprehensive privacy laws during the 2023 legislative sessions that will go into effect in 2024 and beyond, including New Hampshire and New Jersey. Other states will be considering these laws in the future, and Congress has also been debating passing a federal privacy law. There are also states that are specifically regulating health information that may affect our business. For example, Washington state passed a health privacy law in 2023 that will regulate the collection and sharing of health information, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data and additional states (including Vermont) are considering such legislation for 2024. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available under such laws, it is possible that some of our current or future business activities, including certain clinical research, sales and marketing practices and the provision of certain items and services to our customers, could be subject to challenge under one or more of such privacy and data security laws. The heightening compliance environment and the need to build and maintain robust and secure systems to comply with different privacy compliance and/or reporting requirements in multiple jurisdictions could increase the possibility that a healthcare company may fail to comply fully with one or more of these requirements. If our operations are found to be in violation of any of the privacy or data security laws or regulations described above that are applicable to us, or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil and administrative penalties, damages, fines, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a consent decree or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any product candidates we may develop, once approved, are sold in a foreign country, we may be subject to similar foreign laws.

Review and Approval of Medical Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Non-clinical Studies

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical (pharmaco-toxicological) studies must be conducted in compliance with the principles of good laboratory practice (GLP) as set forth in EU Directive 2004/10/EC (unless otherwise justified for certain particular medicinal products – e.g., radio-pharmaceutical precursors for radio-labeling purposes). In particular, non-clinical studies, both *in vitro* and *in vivo*, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical Trial Approval

On January 31, 2022, the new Clinical Trials Regulation (EU) No 536/2014 became effective in the European Union and replaced the prior Clinical Trials Directive 2001/20/EC. The new regulation aims at simplifying and streamlining the authorization, conduct and transparency of clinical trials in the European Union. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one Member State of the European Union, or EU Member State, will only be required to submit a single application for approval. The submission will be made through the Clinical Trials Information System, a new clinical trials portal overseen by the EMA and available to clinical trial sponsors, competent authorities of the EU Member States and the public.

Beyond streamlining the process, the new Regulation includes a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors, and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned). Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned EU Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

The Clinical Trials Regulation, or CTR, foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the Clinical Trials Regulation varies. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR.

Parties conducting certain clinical trials must, as in the United States, post clinical trial information in the European Union at the EU Clinical Trials Register.

Marketing Authorization

To obtain marketing approval of a drug under European Union regulatory systems, a sponsor must submit a marketing authorization application, or MAA, either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all European Union member states. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the European Medicines Agency, or EMA, is responsible for conducting the initial assessment of a drug. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the sponsor in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. In this circumstance, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure is available to sponsors who wish to market a product in various European Union member states where such product has not received marketing approval in any European Union member states before. The decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state designated by the sponsor, known as the reference member state. Under this procedure, a sponsor submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment report and drafts of the related materials within 210 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report and related materials, each concerned member state must decide whether to approve the assessment report and related materials.

If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the European Commission, whose decision is binding on all member states.

Conditional Approval

In particular circumstances, European Union legislation (Article 14–a Regulation (EC) No 726/2004 (as amended by Regulation (EU) 2019/5 and Regulation (EC) No 507/2006 on Conditional Marketing Authorizations for Medicinal Products for Human Use) enables sponsors to obtain a conditional marketing authorization prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional approvals may be granted for product candidates (including medicines designated as orphan medicinal products) if (1) the product candidate is intended for the treatment, prevention or medical diagnosis of seriously debilitating or life-threatening diseases; (2) the product candidate is intended to meet unmet medical needs of patients; (3) a marketing authorization may be granted prior to submission of comprehensive clinical data provided that the benefit of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required; (4) the risk-benefit balance of the product candidate is positive, and (5) it is likely that the sponsor will be in a position to provide the required comprehensive clinical trial data. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization, but applicants can also request EMA to conduct an accelerated assessment, for instance in cases of unmet medical needs.

Periods of Authorization and Renewals

A marketing authorization has an initial validity for five years in principle. The marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the European Union Member State. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. The European Commission or the competent authorities of the European Union Member States may decide, on justified grounds relating to pharmacovigilance, to proceed with one further five-year period of marketing authorization. Once subsequently definitively renewed, the marketing authorization shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the

European Union market (in case of centralized procedure) or on the market of the authorizing European Union Member State within three years after authorization ceases to be valid (the so-called sunset clause).

Regulatory Requirements after a Marketing Authorization has been Obtained

In case an authorization for a medicinal product in the European Union is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- Compliance with the European Union's stringent pharmacovigilance or safety reporting rules must be ensured. These rules can impose post-authorization studies and additional monitoring obligations.

- The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable European Union laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with European Union cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the European Union with the intention to import the active pharmaceutical ingredients into the European Union.

- The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the European Union notably under Directive 2001/83EC, as amended, and European Union Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the European Union.

Regulatory Data Protection in the European Union

In the European Union, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Directive 2001/83/EC. Regulation (EC) No 726/2004 repeats this entitlement for medicinal products authorized in accordance the centralized authorization procedure. Data exclusivity prevents sponsors for authorization of generics of these innovative products from referencing the innovator's data to assess a generic (abridged) application for a period of eight years. During an additional two-year period of market exclusivity, a generic marketing authorization application can be submitted and authorized, and the innovator's data may be referenced, but no generic medicinal product can be placed on the European Union market until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Pediatric Exclusivity

If a sponsor obtains a marketing authorization in all European Union Member States, or a marketing authorization granted in the centralized procedure by the European Commission, and the study results for the pediatric population are included in the product information, even when negative, the medicine is then eligible for an additional six-month period of qualifying patent protection through extension of the term of the Supplementary Protection Certificate, or SPC, or alternatively a one year extension of the regulatory market exclusivity from ten to eleven years, as selected by the marketing authorization holder.

Patent Term Extensions

The European Union also provides for patent term extension through SPCs. The rules and requirements for obtaining a SPC are similar to those in the United States. An SPC may extend the term of a patent for up to five years after its originally scheduled expiration date and can provide up to a maximum of fifteen years of marketing exclusivity for a drug. In certain circumstances, these periods may be extended for six additional months if pediatric exclusivity is obtained. Although SPCs are available throughout the European Union, sponsors must apply on a country-by-country basis. Similar patent term extension rights exist in certain other foreign jurisdictions outside the European Union.

Reimbursement and Pricing of Prescription Pharmaceuticals

In the European Union, similar political, economic and regulatory developments to those in the United States may affect our ability to profitably commercialize our product candidates, if approved. In markets outside of the United States and the European Union, reimbursement and healthcare payment systems vary significantly by country and many countries have instituted price ceilings on specific products and therapies. In many countries, including those of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control and access. 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, pharmaceutical firms may be required to conduct a clinical trial that compares the cost-effectiveness of the product to other available therapies.

Review and Approval of Medical Devices in the European Union

The European Union has adopted numerous directives and standards regulating, among other things, the design, manufacture, clinical trials, labeling, approval and adverse event reporting for medical devices. In the European Union, or the European Union, medical devices must comply with the Essential Requirements in Annex I to the currently applicable European Union Medical Devices Directive (Council Directive 93/42/EEC), or the Essential Requirements. Compliance with these requirements is a prerequisite to be able to affix the CE Mark of Conformity to medical devices, without which they cannot be marketed or sold in the European Economic Area, or EEA, comprised of the European Union member states plus Norway, Iceland, and Liechtenstein.

To demonstrate compliance with the Essential Requirements a manufacturer must undergo a conformity assessment procedure, which varies according to the type of medical device and its classification. Except for low risk medical devices, where the manufacturer can issue a CE Declaration of Conformity based on a self-assessment of the conformity of its products with the Essential Requirements, a conformity assessment procedure requires the intervention of a third-party organization designated by competent authorities of a European Union country to conduct conformity assessments, or a Notified Body. Notified Bodies are independent testing houses, laboratories, or product certifiers typically based within the European Union and authorized by the European member states to perform the required conformity assessment tasks, such as quality system audits and device compliance testing. The Notified Body would typically audit and examine the product's Technical File and the quality system for the manufacture, design and final inspection of the product before issuing a CE Certificate of Conformity demonstrating compliance with the relevant Essential Requirements.

Medical device manufacturers must carry out a clinical evaluation of their medical devices to demonstrate conformity with the relevant Essential Requirements. This clinical evaluation is part of the product's Technical File. A clinical evaluation includes an assessment of whether a medical device's performance is in accordance with its intended use, and that the known and foreseeable risks linked to the use of the device under normal conditions are minimized and acceptable when weighed against the benefits of its intended purpose. The clinical evaluation conducted by the manufacturer must also address any clinical claims, the adequacy of the device labeling and information (particularly claims, contraindications, precautions and warnings) and the suitability of related Instructions for Use. This assessment must be based on clinical data, which can be obtained from clinical studies conducted on the devices being assessed, scientific literature from similar devices whose equivalence with the assessed device can be demonstrated or both clinical studies and scientific literature.

With respect to implantable devices or devices classified as Class III in the European Union, the manufacturer must conduct clinical studies to obtain the required clinical data, unless relying on existing clinical data from similar devices can be justified. As part of the conformity assessment process, depending on the type of devices, the Notified Body will review the manufacturer's clinical evaluation process, assess the clinical evaluation data of a representative sample of the device's subcategory or generic group, or assess all the clinical evaluation data, verify the manufacturer's assessment of that data and assess the validity of the clinical evaluation report and the conclusions drawn by the manufacturer.

Even after a manufacturer receives a CE Certificate of Conformity enabling the CE mark to be placed on it products and the right to sell the products in the EEA countries, a Notified Body or a competent authority may require post-marketing studies of the products. Failure to comply with such requirements in a timely manner could result in the withdrawal of the CE Certificate of Conformity and the recall or withdrawal of the subject product from the European market.

A manufacturer must inform the Notified Body that carried out the conformity assessment of the medical devices of any planned substantial changes to the devices which could affect compliance with the Essential Requirements or the devices' intended purpose. The Notified Body will then assess the changes and verify whether they affect the product's conformity with the Essential Requirements or the conditions for the use of the devices. If the assessment is favorable, the Notified Body will issue a new CE Certificate of Conformity or an addendum to the existing CE Certificate of Conformity attesting compliance with the Essential Requirements. If it is not, the manufacturer may not be able to continue to market and sell the product in the EEA.

In the European Union, medical devices may be promoted only for the intended purpose for which the devices have been CE marked. Failure to comply with this requirement could lead to the imposition of penalties by the competent authorities of the European Union Member States. The penalties could include warnings, orders to discontinue the promotion of the medical device, seizure of the promotional materials and fines. Promotional materials must also comply with various laws and codes of conduct developed by medical device industry bodies in the European Union governing promotional claims, comparative advertising, advertising of medical devices reimbursed by the national health insurance systems and advertising to the general public.

Additionally, all manufacturers placing medical devices in the market in the European Union are legally bound to report any serious or potentially serious incidents involving devices they produce or sell to the competent authority in whose jurisdiction the incident occurred. In the European Union, manufacturers must comply with the European Union Medical Device Vigilance System. Under this system, incidents must be reported to the relevant authorities of the European Union countries, and manufacturers are required to take Field Safety Corrective Actions, or FSCAs, to reduce a risk of death or serious deterioration in the state of health associated with the use of a medical device that is already placed on the market. An incident is defined as any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labeling or the instructions for use which, directly or indirectly, might lead to or might have led to the death of a patient or user or of other persons or to a serious deterioration in their state of health. An FSCA may include the recall, modification, exchange, destruction or retrofitting of the device. FSCAs must be communicated by the manufacturer or its European Authorized Representative to its customers and to the end users of the device through Field Safety Notices.

The legal framework currently applicable for medical devices in the European Union was amended by Medical Devices Regulation (Regulation (EU) 2017/745) adopted in 2017, which we refer to as the MDR and which repeals and replaces the European Union Medical Devices Directive. Unlike directives, which must be implemented into the national laws of the European Economic Area, or EEA, member states, the MDR is directly applicable (i.e., without the need for adoption of EEA member State laws implementing them) in all EEA member states and is intended to eliminate current differences in the regulation of medical devices among EEA member states. The MDR, among other things, is intended to establish a uniform, transparent, predictable and sustainable regulatory framework across the EEA for medical and ensure a high level of safety and health.

The MDR became applicable on May 26, 2021 and will, among other things:

- strengthen the rules on placing devices on the market and reinforce surveillance once they are available;
- establish explicit provisions on manufacturers' responsibilities for the follow-up of the quality, performance and safety of devices placed on the market;
- improve the traceability of medical devices throughout the supply chain to the end-user or patient through a unique identification number;
- set up a central database to provide patients, healthcare professionals and the public with comprehensive information on products available in the European Union; and

- strengthen rules for the assessment of certain high-risk devices, such as implants, which may have to undergo an additional check by experts before they are placed on the market.

Brexit and the Regulatory Framework in the United Kingdom

The UK's withdrawal from the EU took place on January 31, 2020. The EU and the UK reached an agreement on their new partnership in the Trade and Cooperation Agreement, which we refer to as the Agreement and which was applied provisionally beginning on January 1, 2021 and which entered into force on May 1, 2021. The Agreement focuses primarily on free trade by ensuring no tariffs or quotas on trade in goods, including healthcare products such as medicinal products. Thereafter, the EU and the UK will form two separate markets governed by two distinct regulatory and legal regimes. As such, the Agreement seeks to minimize barriers to trade in goods while accepting that border checks will become inevitable as a consequence that the UK is no longer part of the single market. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency (MHRA) became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales. Under the 2023 "Windsor Framework" and related laws, the MHRA became responsible for approving all medicinal products destined for the UK market (i.e., Great Britian and Northern Ireland), effective January 1, 2025. A single UK-wide marketing authorization will be granted by the MHRA for all medicinal products to be sold in the UK, enabling products to be sold in a single pack and under a single authorization throughout the UK. The Human Medicines Regulations 2012 (SI 2012/1916) (as amended) (HMR) is the primary legal instrument for the regulation of medicines in the UK. The HMR has incorporated into the domestic law the body of EU law instruments governing medicinal products that pre-existed prior to the UK's withdrawal from the EU.

EU laws which have been transposed into UK law through secondary legislation continue to be applicable as "retained EU law." However, new legislation such as the (EU) Clinical Trials Regulation will not be applicable in Great Britain. Since a significant proportion of the regulatory framework for pharmaceutical products in the UK covering the quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorizations, commercial sales, and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit may have a material impact upon the regulatory regime with respect to the development, manufacture, importation, approval, and commercialization of our product candidates in the UK. For example, the UK is no longer covered by the centralized procedures for obtaining EU-wide marketing authorizations from the EMA, and a separate marketing authorization will be required to market our product candidates in the UK. A new international recognition framework has been in place since January 1, 2024, whereby the MHRA will have regard to decisions on the approval of marketing authorizations made by the EMA and certain other regulators when determining an application for a new Great Britian marketing authorization.

General Data Protection Regulation

Many countries outside of the United States maintain rigorous laws governing the privacy and security of personal information. The collection, use, disclosure, transfer, or other processing of personal data, including personal health data, regarding individuals who are located in the EEA, and the processing of personal data that takes place in the EEA, is subject to the GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, and it imposes heightened requirements on companies that process health and other sensitive data, such as requiring in many situations that a company obtain the consent of the individuals to whom the sensitive personal data relate before processing such data. Examples of obligations imposed by the GDPR on companies processing personal data that fall within the scope of the GDPR include providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, appointing a data protection officer, providing notification of data breaches and taking certain measures when engaging third-party processors.

The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR is a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance. In July 2020, the Court of Justice of the European Union, or the CJEU, invalidated the European Union-U.S. Privacy Shield framework, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the United States. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EEA to the United States. Following the withdrawal of the UK from the European Union, the UK Data Protection Act 2018 applies to the processing of personal data that takes place in the UK and includes parallel obligations to those set forth by GDPR.

Additionally, in October 2022, President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-U.S. Privacy Shield. The EU initiated the process to adopt an adequacy decision for the EU-U.S. Data Privacy Framework in December 2022 and the European Commission adopted the adequacy decision on July 10, 2023. The adequacy decision will permit U.S. companies who self-certify to the EU-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the EU to the U.S. However, some privacy advocacy groups have already suggested that they will be challenging the EU-U.S. Data Privacy Framework. If these challenges are successful, they may not only impact the EU-U.S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales of products will depend, in part, on the extent to which the costs of the products will be covered by third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication. Additionally, the containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on investment in product development.

Section 1833(t)(6) of the Social Security Act provides for temporary additional payments or "transitional pass-through payments" for certain drugs and biological agents. As originally enacted by the Balanced Budget Refinement Act of 1999, this provision required Centers for Medicare and Medicaid Services, or CMS, to make additional payments to hospitals for current orphan drugs, as designated under section 526 of the FDCA; current drugs and biological agents and brachytherapy sources used for the treatment of cancer; and current radiopharmaceutical drugs and biological products. Transitional pass-through payments are also provided for certain new drugs, devices and biological agents that were not paid for as a hospital outpatient department service as of December 31, 1996, and whose cost is "not insignificant" in relation to the Outpatient Prospective Payment System, or OPPS, payment for the procedures or services associated with the new drug, device, or biological. Under the statute, transitional pass-through payments can be made for at least two years but not more than three years.

J-Codes are part of the Healthcare Common Procedure Coding System (HCPCS) Level II set of procedure codes. These codes are used by CMS and other managed care organizations to identify drugs that ordinarily cannot be self-administered by a patient. Lacrimal ophthalmic inserts containing dexamethasone, such as DEXTENZA, have a specific and permanent J-Code, J1096, that allows for a simpler and more convenient reimbursement process versus miscellaneous J-codes. Since its launch, DEXTENZA has been payable in ASCs and HOPDs separately from ophthalmic surgery via the transitional pass-through status under the J1096 J-Code. However, the pass-through status for J1096 ended on December 31, 2022. In November 2022, as part of the annual CMS rule-making cycle, the CY 2023 OPPS rule was finalized and provided that DEXTENZA would qualify under the criteria established for non-opioid pain management drugs as a surgical supply provision. This provision allows for continued separate payment of DEXTENZA in the ASC setting for 2023 but does not require separate payment for DEXTENZA in the HOPD setting.

CPT codes are part of the HCPCS Level I set of procedure codes which consists of codes that are used to report medical services and procedures furnished by physicians. These codes are also used by CMS and other managed care organizations. Drug-eluting intracanalicular inserts, such as DEXTENZA, have a procedure-specific and permanent Category 1 CPT code, 68841, used to facilitate reimbursement for the administration of inserts into the canaliculus. In 2023, the Medicare Physician Fee Schedule, or MPFS, for the insertion of DEXTENZA into the canaliculus was $32.53 in the ASCs and $38.29 in the physician's office for unilateral insertion. In November 2023, the CY 2024 MPFS rule was finalized resulting in a marginal decrease in physician payments compared to 2023 to $31.43 in the ASCs and $37.33 in the physician's office for unilateral insertion, due to a decrease in the conversion factor which CMS uses to translate the relative value units, or RVUs, of medical services into fee schedule payment amounts. The RVU for code 68841 was unchanged.

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

Healthcare Law and Regulation

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse and other healthcare laws and regulations. Such restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;

- the federal False Claims Act imposes civil penalties, and provides for civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, including the Final Omnibus Rule published in January 2013, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal false statements statute prohibits 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;

- the Foreign Corrupt Practices Act, or FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;

- the federal transparency requirements under the ACA, known as the federal Physician Payments Sunshine Act, will require certain manufacturers of drugs, devices, biologics and medical supplies to report to CMS within the HHS information related to payments and other transfers of value to physicians, other healthcare providers and teaching hospitals and physician ownership and investment interests held by physicians and their immediate family members; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers.

Violations of these laws are punishable by criminal and/or civil sanctions, including, in some instances, exclusion from participation in federal and state health care programs, such as Medicare and Medicaid. Ensuring compliance is time consuming and costly. Similar healthcare laws and regulations exist in the EU and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers and laws governing the privacy and security of personal information.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of drug and biologic products, limiting coverage and reimbursement for medical products and other changes to the healthcare system in the United States.

In March 2010, the United States Congress enacted the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the PPACA, which, among other things, includes changes to the coverage and payment for pharmaceutical products under government healthcare programs. Other legislative changes have been proposed and adopted since the PPACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031. Pursuant to the Coronavirus Aid, Relief and Economic Security Act, or CARES Act, and subsequent legislation, these Medicare sequester reductions have been suspended and reduced through the end of June 2022, with the full 2% cut resuming thereafter. Under current legislation, the actual reductions in Medicare payments may vary up to 4%.

Since enactment of the PPACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, or the Tax Act, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. On December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the PPACA is an essential and inseverable feature of the PPACA, and therefore because the mandate was repealed as part of the Tax Act, the remaining provisions of the PPACA are invalid as well.

The U.S. Supreme Court heard this case on November 10, 2020 and, on June 17, 2021, dismissed this action after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the PPACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the PPACA, including directing federal agencies with authorities and responsibilities under the PPACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the PPACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden rescinded those orders and issued a new executive order that directs federal agencies to reconsider rules and other policies that limit access to healthcare, and consider actions that will protect and strengthen that access. Under this order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the PPACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and under the PPACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

Pharmaceutical Prices

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, President Trump issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, CMS issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. The final rule is currently the subject of ongoing litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by the FDA. Further, on November 20, 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 final rule would eliminate the current safe harbor for Medicare drug rebates and create new safe harbors for beneficiary point-of-sale discounts and pharmacy benefit manager, or PBM, service fees. It originally was set to go into effect on January 1, 2022, but with passage of the Inflation Reduction Act, or IRA, has been delayed by Congress to January 1, 2032.

On July 9, 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. The Executive Order directs the HHS to create a plan within 45 days to combat "excessive pricing of prescription pharmaceuticals and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such pharmaceuticals, and to address the recurrent problem of price gouging." On September 9, 2021, HHS released its plan to reduce pharmaceutical prices. The key features of that plan are to: (a) make pharmaceutical prices more affordable and equitable for all consumers and throughout the health care system by supporting pharmaceutical price negotiations with manufacturers; (b) improve and promote competition throughout the prescription pharmaceutical industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

More recently, on August 16, 2022, the IRA was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated “maximum fair price” under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. A number of states, for example, require drug manufacturers and other entities in the drug supply chain, including health carriers, pharmacy benefit managers, wholesale distributors, to disclose information about pricing of pharmaceuticals. In addition, regional healthcare organizations and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription pharmaceutical and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Human Capital

As of December 31, 2023, we had 267 full-time employees. The following table provides an overview of the distribution of those employees:

Department	Headcount
Research & Development	118
Sales & Marketing	94
Manufacturing	14
General & Administrative	41
Total Employees	267

We are committed to inclusion and diversity and believe that these are important elements of our culture that enables us to attract and retain a high quality workforce.

The development, attraction and retention of employees is a critical success factor for us for the execution of our business strategy and succession planning. To support the advancement of our employees, we offer training and development programs encouraging advancement from within and continue to fill our team with strong and experienced management talent. We leverage both formal and informal programs to identify, foster, and retain top talent at both the corporate and operating unit level.

We provide employee wages and benefits that we believe are competitive and consistent with the employee positions, skill levels, experience, knowledge and geographic location. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

We value the health, safety and wellbeing of our employees and their families. As an example, in response to the COVID-19 pandemic, we implemented significant changes that we determined were in the best interest of our employees, which included allowing a number of our corporate employees to work remotely, as appropriate.

Our Corporate Information

We were incorporated under the laws of the State of Delaware in 2006. Our principal executive offices are located at 15 Crosby Drive, Bedford, MA 01730, and our telephone number is (781) 357-4000. Our manufacturing is located at 36 Crosby Drive, Suite 101, Bedford, MA 01730 and our research and development operations are located at 15 Crosby Drive, Bedford, MA 01730. Our website address is www.ocutx.com.

Available Information

We make available free of charge through our website our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act. We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the SEC. We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. The information contained on, or that can be access through, our website is not a part of or incorporated by reference in this Annual Report on Form 10-K.

Item 1A. Risk Factors.

The following risk factors and other information included in this Annual Report on Form 10-K, including under the heading "Summary of Risk Factors" in this Annual Report, should be carefully considered. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see the section of this Annual Report on Form 10-K captioned "Forward-Looking Statements" for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to Our Financial Position and Need for Additional Capital

We have a history of incurring significant losses. We expect to incur losses over the next several years and may never achieve or maintain profitability.

We have a history of incurring significant losses. Our net losses were $80.7 million and $71.0 million for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023, we had an accumulated deficit of $697.6 million. We have financed our operations primarily through private placements of our preferred stock, public offerings and private placements of our common stock, borrowings under our credit facilities, including $82.5 million under a credit and security agreement, or the Barings Credit Agreement, with Barings Finance LLC, or Barings, as administrative agent, and the lenders party thereto, which we refer to as the Barings Credit Facility, the private placement of convertible notes in the aggregate principal amount of our $37.5 million, or the Convertible Notes, and sales of our products. We have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and clinical trials, and the commercialization of DEXTENZA. Although we expect to continue to generate revenue from sales of DEXTENZA, we expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year.

We anticipate we will incur substantial expenses if and as we:

- continue our ongoing clinical trials, including our pivotal Phase 3 clinical trial of AXPAXLI, which we refer to as the SOL-1 trial, for the treatment of wet age-related macular degeneration, or wet AMD; the HELIOS trial of AXPAXLI for the treatment of non-proliferative diabetic retinopathy, or NPDR; our Phase 2 clinical trial of PAXTRAVA for the reduction of IOP in patients with primary open-angle glaucoma, or OAG, or ocular hypertension, or OHT; and our Phase 2 clinical trial of OTX-DED for the short-term treatment of the signs and symptoms of dry eye disease;
- continue to monitor subjects according to the applicable clinical trial protocols in our clinical trials that have been completed, including our clinical trial to evaluate DEXTENZA in pediatric subjects following cataract surgery;
- determine to initiate new clinical trials to evaluate our product candidates, including our planned second pivotal Phase 3 clinical trial of AXPAXLI for the treatment of wet AMD, which we refer to as the SOL-2 trial; our planned pivotal Phase 3 clinical trial of AXPAXLI for the treatment of NPDR; and, subject to our evaluation of strategic alternatives, possible pivotal clinical trials of PAXTRAVA for the reduction of IOP in patients with primary OAG or OHT;
- continue to commercialize DEXTENZA in the United States;
- continue to develop and expand our sales, marketing and distribution capabilities for DEXTENZA and any other products or product candidates we intend to commercialize;
- conduct or support research and development activities on, and seek regulatory approvals for, DEXTENZA and PAXTRAVA in specified Asian markets pursuant to our license agreement and collaboration with AffaMed Therapeutics Limited, or AffaMed;
- continue the research and development of our other product candidates;
- seek to identify and develop additional product candidates;
- seek marketing approvals for any of our product candidates that successfully complete clinical development;
- scale up our manufacturing processes and capabilities to support sales of commercial products, clinical trials of our product candidates and commercialization of any of our product candidates for which we obtain marketing approval, and expand our facilities to accommodate this scale up and any corresponding growth in personnel;
- renovate our existing facilities including research and development laboratories, manufacturing space and office space;
- maintain, expand and protect our intellectual property portfolio;
- expand our operational, financial, administrative and management systems and personnel, including personnel to support our clinical development, manufacturing and commercialization efforts;
- defend ourselves against legal proceedings, if any;
- make investments to improve our defenses against cybersecurity and establish and maintain cybersecurity insurance;
- increase our product liability and clinical trial insurance coverage as we expand our clinical trials and commercialization efforts; and
- continue to operate as a public company.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. Our development expenses will increase if:

- we are required by the FDA or the other regulatory authorities to perform trials or studies in addition to those currently expected;
- there are any delays in receipt of regulatory clearance to begin our planned clinical programs;
- there are any delays in enrollment of subjects in or completion of our clinical trials or the development of our product candidates; or
- there are any delays in receiving marketing approval of any of our product candidates.

For us to become and remain profitable, we will need to continue to successfully commercialize DEXTENZA and to successfully develop and commercialize other products with significant market potential. This will require us or our current or future collaborators to be successful in a range of challenging activities, including:

- continuing to commercialize DEXTENZA in the United States, including by further developing our manufacturing, marketing, sales force, and distribution capabilities;
- completing clinical development of our product candidates, including AXPAXLI, PAXTRAVA, OTX-DED, and OTX-CSI;
- obtaining marketing approval for these product candidates;
- manufacturing, marketing, selling and distributing any other products for which we obtain marketing approval;
- achieving an adequate level of market acceptance of and obtaining and maintaining coverage and adequate reimbursement from Centers for Medicare and Medicaid Services, or CMS, and other third-party payors for our products; and
- protecting our rights to our intellectual property portfolio.

Even if we succeed in our commercialization efforts, we may never generate revenue that is sufficient to achieve profitability. We do not anticipate revenue from sales of DEXTENZA for the treatment of ocular inflammation and pain following ophthalmic surgery and ocular itching associated with allergic conjunctivitis will be sufficient for us to become profitable for several years, if ever.

Even 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 depress the value of our common stock and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment.

We will need substantial additional funding. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or commercialization efforts.

We expect to devote substantial financial resources to our ongoing and planned activities, particularly if and as we advance AXPAXLI, PAXTRAVA, OTX-DED and OTX-CSI through clinical development, and continue to commercialize DEXTENZA for the treatment of ocular inflammation and pain following ophthalmic surgery and for the treatment of ocular itching associated with allergic conjunctivitis. We expect to devote substantial financial resources as we conduct late-stage clinical trials for our product candidates, seek marketing approval for any such product candidate for which we obtain favorable pivotal clinical results, and commercialize any products for which we receive marketing approval. In addition, we plan to devote significant financial resources to conduct research and development of our other product candidates. Accordingly, we will need to obtain substantial additional funding to fully support our continuing and planned operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or commercialization efforts.

As of December 31, 2023, we had cash and cash equivalents of $195.8 million, outstanding debt with a principal amount of $82.5 million under the Barings Credit Facility, and $37.5 million aggregate principal amount of Convertible Notes plus accrued interest of $10.9 million. Based on our current operating plan, which includes estimates of anticipated cash inflows from DEXTENZA product sales and cash outflows from operating expenses and capital expenditures and reflects our observance of the minimum liquidity covenant of $20.0 million under the Barings Credit Agreement, we believe that our existing cash and cash equivalents as of December 31, 2023, plus the cash received from a private placement of our common stock in February 2024 of $325.0 million before deducting placement agent fees and other offering expenses, will enable us to fund our planned operating expenses, debt service obligations and capital expenditure requirements at least into 2028. These estimates are subject to various assumptions, including assumptions as to the revenues and expenses associated with the commercialization of DEXTENZA, the pace of our research and clinical development programs, the timing of commencement of dosing and enrollment of our clinical trials, and other aspects of our business. We have based our estimates on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Our future capital requirements will depend on many factors, including:

- the level of product sales from DEXTENZA and any additional products for which we obtain marketing approval in the future and the level of third-party reimbursement of such products;
- the costs of sales, marketing, distribution and other commercialization efforts with respect to DEXTENZA and any additional products for which we obtain marketing approval in the future, including costs increases due to inflation;
- the progress, costs and outcome of our ongoing and planned clinical trials of our product candidates, in particular AXPAXLI for the treatment of wet AMD and NPDR, and, subject to our evaluation of strategic alternatives, PAXTRAVA for the treatment of OAG or OHT;
- the scope, progress, costs and outcome of preclinical development and clinical trials of our other product candidates;
- the costs, timing and outcome of regulatory review of our product candidates by the FDA, the EMA or other regulatory authorities;
- the costs of scaling up our manufacturing processes and capabilities to support sales of commercial products, clinical trials of our product candidates and commercialization of any of our product candidates for which we obtain marketing approval and of expanding our facilities to accommodate this scale up and any corresponding growth in personnel;
- the extent of our debt service obligations and our ability, if desired, to refinance any of our existing debt on terms that are more favorable to us;
- the amounts we are entitled to receive, if any, as reimbursements for clinical trial expenditures, development, regulatory, and sales milestone payments, and royalty payments under our license agreement with AffaMed;
- the extent to which we choose to establish additional collaboration, distribution or other marketing arrangements for our products and product candidates;
- the costs and outcomes of any legal actions and proceedings;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and
- the extent to which we acquire or invest in other businesses, products and technologies.

Conducting preclinical testing and clinical trials, seeking market approvals and commercializing products are time-consuming, expensive and uncertain processes that take years to complete. We may never generate the necessary data or results required to obtain regulatory approval of products with the market potential sufficient to enable us to generate significant revenues from the sale of such products. Accordingly, we will need to obtain substantial additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or products or product candidates.

Until such time, if ever, as we can generate product revenues sufficient to achieve profitability, we expect to finance our cash needs through equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements, royalty agreements, and marketing and distribution arrangements. We do not have any committed external source of funds, although our license agreement with AffaMed provides for AffaMed's reimbursement of certain clinical expenses incurred by us in connection with our collaboration and for our potential receipt of development and sales milestone payments and royalty payments. To the extent that we raise additional capital through the sale of equity, preferred equity or convertible debt securities, our securityholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our existing securityholders' rights as holders or beneficial owners of our common stock. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Our pledge of our assets as collateral to secure our obligations under the Barings Credit Facility pursuant to which we have a total borrowing capacity of $82.5 million, which has been fully drawn down, may limit our ability to obtain additional debt or other financing.

If we raise additional funds through collaborations, strategic alliances, licensing arrangements, royalty agreements or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, products or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

Our substantial indebtedness may limit cash flow available to invest in the ongoing needs of our business or otherwise affect our operations.

On August 2, 2023, we entered into the Barings Credit Agreement providing for the Barings Credit Facility in the aggregate principal amount of $82.5 million. Under the Barings Credit Facility we have $82.5 million, net of unamortized discount and fees, of outstanding principal indebtedness. Under the Barings Credit Agreement, we are permitted to make payments of interest and fees only through August 2029, at which time we will be required to repay the full principal amount in addition to any outstanding interest and fees. In addition, we are obligated to pay a fee, which we refer to as the Royalty Fee, in an amount equal to $82.5 million, reduced by the total amount of interest and principal prepayment fees paid by us and subject to further potential reductions as specified in the Barings Credit Agreement. We are required to pay the Royalty Fee in installments to Barings, for the benefit of the lenders, on a quarterly basis in an amount equal to three and one-half percent (3.5%) of the net sales of DEXTENZA occurring during such quarter, subject to the terms, conditions and limitations specified in the Barings Credit Agreement, until the Royalty Fee is paid in full. The Royalty Fee is due and payable upon a change of control of the company. The Royalty Fee may also be reduced if a change of control or a sale of all or substantially all of our assets occurs within the first twelve months of the term of the Barings Credit Agreement.

Our obligations under the Barings Credit Agreement are secured by all of our assets, including our intellectual property. The Barings Credit Facility includes negative covenants restricting us from making payments to the holders of our outstanding Convertible Notes, except in connection with a proposed conversion to equity and with respect to certain permitted expenses and requiring us to maintain a minimum liquidity amount of $20.0 million. The Barings Credit Agreement also includes customary affirmative and negative covenants.

In March 2019, we issued $37.5 million aggregate principal amount of issued and outstanding Convertible Notes. The Convertible Notes mature on a date 91 days following the maturity of the indebtedness under the Barings Credit

Facility, and interest on the Convertible Notes is payable at maturity or if earlier converted, repurchased or redeemed pursuant to their terms. We could in the future incur additional indebtedness beyond such amounts, including by potentially amending the Barings Credit Agreement.

Our substantial debt combined with our other financial obligations and contractual commitments could have significant adverse consequences, including:

- requiring us to dedicate a substantial portion of cash and cash equivalents and marketable securities to the payment of interest on, and principal of, our debt and related fees such as the Royalty Fee, which collectively reduce the amounts available to fund operating expenditures, including working capital, and capital expenditures and other general corporate purposes and may also have the effect of delaying, deferring or preventing a change of control;

- obligating us to additional negative covenants further restricting our activities;

- limiting our flexibility in planning for, or reacting to, changes in our business and our industry; and

- placing us at a competitive disadvantage compared to our competitors that have less debt or better debt servicing options.

We intend to satisfy our current and future debt service obligations with our existing cash and cash equivalents, anticipated product revenue from DEXTENZA and funds from external sources. However, we may not have sufficient funds or may be unable to arrange for additional financing to pay the amounts due under our existing debt. Funds from external sources may not be available on acceptable terms, if at all.

A failure to comply with conditions of our Barings Credit Agreement or the Convertible Notes could result in an event of default under those instruments. The Barings Credit Agreement and Convertible Notes also have cross-default provisions, pursuant to which a default under one instrument could cause a default in others. In an event of default, including upon the occurrence of an event that would reasonably be expected to have a material adverse effect on our business or operations, the amounts due under our Barings Credit Agreement or the Convertible Notes could accelerate. As a result, we may not have sufficient funds or may be unable to arrange for additional financing to repay our indebtedness or to make any accelerated payments, and the lenders could seek to enforce security interests in the collateral securing such indebtedness.

We hold our cash and cash equivalents that we use to fund our operating expenses, debt service obligations, and capital expenditure requirements in deposit accounts that could be adversely affected if the financial institutions holding such funds fail.

We hold our cash and cash equivalents that we use to fund our operating expenses, debt service obligations, and capital expenditure requirements in deposit accounts at two financial institutions. The balances held in these accounts typically exceeds the standard deposit insurance limit of the Federal Deposit Insurance Corporation, or FDIC. If a financial institution in which we hold such funds fails or is subject to significant adverse conditions in the financial or credit markets, we could be subject to a risk of loss of all or a portion of our uninsured funds or be subject to a delay in accessing all or a portion of such funds. Any such loss or lack of access to these funds could adversely impact our short-term liquidity and ability to meet our operating expense, debt service, and capital expenditure obligations.

For example, on March 10, 2023, Silicon Valley Bank, or SVB, was closed by the California Department of Financial Protection and Innovation, and the FDIC was appointed as receiver. During this time, deposits held at SVB were temporarily inaccessible to SVB's customers. At the time SVB was closed by its regulators, we maintained a significant portion of our cash and cash equivalents in deposit accounts with SVB.

Our cash and cash equivalents remain concentrated in a small number of financial institutions. If any of the financial institutions in which we hold cash or cash equivalents were to fail in the future, we cannot provide any assurances that any governmental agencies would take action to protect or provide access to our uninsured deposits, or a third party would assume the failing financial institution's obligations, in a similar manner as occurred in connection with the closure, receivership, and sale of SVB, and we may lose or be unable to access some or all of the uninsured funds we are holding at such financial institution.

We also maintain investment accounts with multiple financial institutions. If our access to our cash and cash equivalents in our deposit accounts is impaired, we may not be able to open new operating accounts or to sell investments or transfer funds from our investment accounts to new operating accounts on a timely basis sufficient to meet our operating expense, debt service, and capital expenditure obligations.

We might not be able to utilize a significant portion of our net operating loss carryforwards and research and development tax credit carryforwards.

As of December 31, 2023, we had net operating loss, or NOL, carryforwards for federal and state income tax purposes of $482.6 million and $343.8 million, respectively. The federal and state NOLs generated for annual periods prior to January 1, 2018 begin to expire in 2026. Our federal NOLs generated for the years ended after December 31, 2018, which amounted to a total of $356.8 million, can be carried forward indefinitely. As of December 31, 2023, we also had available research and development tax credit carryforwards for federal and state income tax purposes of $15.4 million and $8.8 million, respectively, which begin to expire in 2026 and 2025, respectively. These NOL and tax credit carryforwards could expire unused and be unavailable to offset our future income tax liabilities. Even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes because, among other reasons, federal tax rates and the rules governing NOL carryforwards might change; state NOLs generated in one state cannot be used to offset income generated in another state; and the use of NOL carryforwards might become subject to annual limitations under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, and similar state provisions.

Risks Related to Product Development

Clinical trials of our product candidates may not be successful. If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of the FDA or other regulatory authorities or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be delayed or unable to complete, the development and commercialization of such product candidate and our business may be harmed.

Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, including our lead product candidate AXPAXLI, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later stage clinical trials, interim results of a clinical trial do not necessarily predict final results and results from one completed clinical trial may not be replicated in a subsequent clinical trial with a similar study design. Some of our completed studies were conducted with small patient populations, making it difficult to predict whether the favorable results that we observed in such studies will be repeated in larger and more advanced clinical trials. Some of our clinical trials also were conducted with different formulations than those that we are currently evaluating. For example, we are using a single optimized implant of AXPAXLI with a drug load of 450 µg of a more soluble form of axitinib in our SOL-1 trial and intend to use the same formulation in future clinical trials of AXPAXLI including our planned SOL-2 trial. As we have not evaluated this formulation in earlier trials, it may not demonstrate the efficacy or safety profile that we anticipate.

Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. The protocols for our clinical trials and other supporting information are subject to review by the FDA and regulatory authorities outside the United States. However, the FDA is not obligated to comment on our trial protocols within any specified time period or at all or to affirmatively clear or approve our planned pivotal clinical trials. Subject to a waiting period of 30 days, we could choose to initiate our pivotal clinical trials in the United States without waiting for any additional period for comments from the FDA. Although the FDA may provide comments or clear our clinical trial protocols, final determinations for marketing application approval are made after a complete review of a marketing application and are based on the entirety of the data in the new drug application. Furthermore, we are conducting our SOL-1 trial of AXPAXLI under a Special Protocol Assessment, or SPA, agreed to by the FDA. An SPA agreement indicates concurrence by the FDA with the adequacy and acceptability of specific critical elements of the overall protocol design for a clinical trial intended to support a future marketing application, but it does not indicate FDA concurrence on every protocol detail. Moreover, the FDA retains significant discretion in interpreting the terms of an SPA agreement and the data and results from any trial that is the subject of an SPA agreement. An SPA agreement does not ensure the receipt of marketing approval by the FDA or other regulatory authorities or that the approval process will be faster than conventional procedures.

We have devoted a significant portion of our financial resources and business efforts to the development of DEXTENZA and our product candidates. We are currently investing substantial resources to advance the development of AXPAXLI for the treatment of wet AMD and NPDR, PAXTRAVA for the treatment of OAG or OHT, OTX-CSI for the chronic treatment of dry eye disease, and OTX-DED for the short-term treatment of the signs and symptoms of dry eye disease. We currently have several ongoing clinical trials, including our SOL-1 trial, the HELIOS trial, and our Phase 2 clinical trial of PAXTRAVA. We also continue to wind down our post-trial monitoring and surveillance obligations in our Phase 1 clinical trials of AXPAXLI in wet AMD in Australia and the United States and our Phase 3 clinical trial of DEXTENZA in pediatric subjects following cataract surgery.

We have, however, experienced the uncertainty of clinical trials in our own development programs. In our Phase 2 clinical trial for OTX-CSI for the treatment of dry eye disease, for example, OTX-CSI did not meet the primary endpoint of the clinical trial. The trial was designed to evaluate safety, tolerability, durability, and efficacy of two different formulations of OTX-CSI by measuring signs and symptoms of dry eye disease in 140 subjects treated in both eyes over approximately 16 weeks (a 12-week study period, with an additional 4-week safety follow-up). The four groups evaluated in this study were: OTX-CSI for a shorter duration, OTX-CSI for a longer duration, vehicle insert for a longer duration and vehicle insert for a very short duration. The study did not show separation between the OTX-CSI treated subjects (both formulations) and the vehicle treated subjects (both formulations) for the primary endpoint of increased tear production at 12 weeks as measured by the Schirmer's Test.

If clinical trials of any product candidate that we develop fail to demonstrate safety and efficacy to the satisfaction of the FDA or other regulatory authorities or do not otherwise produce clear or favorable results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of such product candidate. We cannot accurately predict when or if any of our product candidates will prove effective or safe in humans or whether our product candidates will receive marketing approval or reach successful commercialization. Our ability to generate product revenues sufficient to achieve profitability will depend heavily on our development and commercialization of products with significant market potential.

If we experience any of a number of possible unforeseen events in connection with our clinical trials, potential marketing approval or commercialization of our product candidates could be delayed or prevented.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;

- the number of subjects required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;

- our third-party contractors may fail to comply with regulatory requirements or meet their obligations to us in a timely manner, or at all;

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;

- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;

- we may decide, or regulators or institutional review boards may require us, to suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;

- the cost of clinical trials of our product candidates may be greater than we anticipate; and
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate.

From time to time, we may decide to conduct clinical trials to assess subjects' clinical response to treatment and choose not to power such trials to measure the applicable efficacy endpoints with statistical significance, as we did in our Phase 2 clinical trials of our former product candidate OTX-TP for the treatment of OAG or OHT. In addition, post-hoc analyses such as those that we performed on certain results of Phase 2 clinical trials of OTX-TP may not be predictive of success in future clinical trials, including as a result of differences in trial design. Post-hoc analyses performed using an unlocked clinical trial database can also result in the introduction of bias and are given less weight by regulatory authorities than pre-specified analyses.

The FDA may also require that New Drug Application, or NDA, submissions for our product candidates include pediatric data. Under the Pediatric Research Equity Act, or PREA, an NDA, a biological licensing application, or BLA, or supplement to an NDA or BLA for certain drugs and biological products must contain data to assess the safety and effectiveness of the drug or biological product in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, unless the sponsor receives a deferral or waiver from the FDA. The applicable legislation in the European Union also requires sponsors to either conduct clinical trials in a pediatric population in accordance with a Pediatric Investigation Plan approved by the Pediatric Committee of the European Medicines Agency, or EMA, or to obtain a waiver or deferral from the conduct of these studies by this Committee. For any of our product candidates for which we are seeking regulatory approval in the United States or the European Union, we cannot guarantee that we will be able to obtain a waiver or alternatively complete any required studies and other requirements in a timely manner, or at all, which could result in associated reputational harm and subject us to enforcement action.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, such as the FDA's requirement that we provide pediatric data for DEXTENZA for the treatment of post-surgical ocular inflammation and pain following cataract surgery prior and for the treatment of ocular itching associated with allergic conjunctivitis in connection with the approval of our NDA for DEXTENZA for those indications, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not favorable or are only modestly favorable or if there are safety concerns, we may:

- be delayed in obtaining or unable to obtain marketing approval for our product candidates;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in testing or marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates.

If we experience delays or difficulties in the enrollment of subjects in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates, or other product candidates that we might develop if we are unable to locate and enroll a sufficient number of eligible subjects to participate in these trials as required by the FDA, the EMA or similar regulatory authorities outside the United States. Although there is a significant prevalence of disease in the areas of ophthalmology in which we are focused, we may nonetheless experience unanticipated difficulty with subject enrollment. For example, in the third quarter of 2017, we initiated a Phase 1 clinical trial of PAXTRAVA outside the United States. After several months, after not enrolling any subjects, we closed this trial in the second quarter of 2018. Additionally, we intended to initiate our Phase 1 clinical trial of AXPAXLI outside the United States in 2018, but delays in enrollment prevented us from dosing subjects until the first quarter of 2019.

A variety of factors affect subject enrollment, including:

- the prevalence and severity of the ophthalmic disease or condition under investigation;
- the design and eligibility criteria for the study in question;
- the perceived risks and benefits of the product candidate under study;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- the proximity and availability of clinical trial sites for prospective subjects;
- actual or threatened public health emergencies or outbreaks of disease (including, for example, the COVID-19 pandemic);
- the conduct of clinical trials by competitors for product candidates that treat the same indications as our product candidates; and
- the lack of adequate compensation for prospective subjects.

Delays can be more pronounced with later-stage clinical trials because they tend to be larger than early-stage trials. For example, enrollment in our Phase 3 clinical trial to evaluate DEXTENZA in pediatric subjects following cataract surgery, to fulfill FDA post-approval regulatory requirements, proceeded more slowly than we had anticipated due to the relative scarcity of pediatric cataract surgical subjects. In addition, we may experience delays in enrollment due to the design of our trials. For example, to qualify for enrollment in the SOL-1 trial, participants receive two aflibercept injections in the screening period and would need to gain at least 10 ETDRS letters from the initial screening visit to Day 1 or achieve a visual acuity of approximately 20/20 or better at Day 1, in addition to satisfying other criteria. Enrollment delays may also arise in our SOL-1 trial due to a reluctance of physicians to enroll subjects in the trial given the novel design being used.

Our inability to enroll a sufficient number of subjects in any of our clinical trials would result in significant delays, could require us to abandon one or more clinical trials altogether and could delay or prevent our receipt of necessary regulatory approvals. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which could cause the value of our common stock to decline and limit our ability to obtain additional financing.

If serious adverse or unacceptable side effects are identified during the development of our product candidates or any other product candidates that we may develop, we may need to abandon or limit our development of such product candidates.

If any of our product candidates are associated with serious adverse events or undesirable side effects in clinical trials or have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the serious adverse events, undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective.

Many compounds that initially showed promise in clinical or early-stage testing for treating ophthalmic disease have later been found to cause side effects that prevented further development of the compound. In addition, adverse events which had initially been considered unrelated to the study treatment may later be found to be caused by the study treatment.

We may not be successful in our efforts to develop additional products and product candidates based on our bioresorbable hydrogel-based formulation technology ELUTYX.

We are currently directing most of our development efforts towards applying our proprietary, bioresorbable hydrogel-based formulation technology ELUTYX to products and product candidates that are designed to provide local programmed-release hydrogel-based therapeutic agents to the eye using active pharmaceutical ingredients that are currently used in FDA-approved ophthalmic drugs. We have a number of product candidates at various stages of development based on ELUTYX and are exploring the potential use of ELUTYX for other ophthalmic diseases and conditions. These product candidates include intracanalicular inserts eluting drug product to the ocular surface; hydrogel drug delivery implants designed to release therapeutic antibodies and small molecules such as TKIs to modulate the biological activity of VEGF over a sustained period following administration by an intravitreal injection for the treatment of diseases and conditions of the back of the eye, including wet AMD and NPDR; and hydrogel drug delivery implants designed to release drug product into the anterior chamber of the eye via an intracameral injection for the treatment of diseases and conditions of the front of the eye.

Our product candidates and any other product candidates that we may develop based on ELUTYX may not be suitable for continued preclinical or clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize products and product candidates that are based on ELUTYX, we will not be able to obtain substantial product revenues in future periods.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. In addition, if we do not accurately evaluate the commercial potential of a target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We are currently prioritizing the advancement of AXPAXLI through Phase 3 clinical development for the treatment of wet AMD and the advancement of AXPAXLI through Phase 1 clinical development for the treatment of NPDR. We are also focused on the advancement through Phase 2 clinical development of PAXTRAVA for the treatment of OAG or OHT, and the continued commercialization of DEXTENZA, and are assessing the further development of OTX-DED for the short-term treatment of the signs and symptoms of dry eye disease and OTX-CSI for the chronic treatment of dry eye disease. Although we believe our prioritization of resources is currently the best use of our resources, we may not be correct.

We have conducted, and may in the future conduct, clinical trials for product candidates at sites outside the United States, and the FDA may not accept data from trials conducted in such locations.

We have conducted, and may in the future choose to conduct, one or more of our clinical trials outside the United States. We are currently conducting the SOL-1 trial both inside and outside of the United States, with planned sites in Argentina and other countries. We have often conducted our initial and earlier-stage clinical trials for our product candidates outside the United States, including our Phase 1 clinical trial for our product candidate AXPAXLI for the treatment of wet AMD in Australia.

Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of this data is subject to conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with ethical principles. The trial population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will depend on its determination that the trials also complied with all applicable U.S. laws and regulations. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and would delay or permanently halt our development of the applicable product candidates. Even if the FDA accepted such data, it could require us to modify our planned clinical trials to receive clearance to initiate such trials in the United States or to continue such trials once initiated.

Other risks inherent in conducting international clinical trials include:

- foreign regulatory requirements, differences in healthcare services, and differences in cultural customs that could restrict or limit our ability to conduct our clinical trials;
- administrative burdens of conducting clinical trials under multiple sets of foreign regulations;
- foreign exchange fluctuations;
- diminished protection of intellectual property in some countries; and
- political and economic risks relevant to foreign countries.

Risks Related to Commercialization

We depend heavily on the success of DEXTENZA and any product candidates for which we may obtain marketing approval. If we fail to commercialize these products successfully, our ability to generate significant product revenues and our business would be materially harmed.

The commercial success of DEXTENZA and any other product candidate for which we obtain marketing approval will depend on many factors, including the following:

- successful completion of preclinical studies and clinical trials;
- applying for and receiving and maintaining marketing approvals from applicable regulatory authorities;
- scaling up our manufacturing processes and capabilities to support commercialization efforts;
- developing, validating and maintaining a commercially viable manufacturing process that is compliant with current good manufacturing practices, or cGMP;
- developing our sales, marketing and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- partnering successfully with our current and future collaborators;
- gaining acceptance of our products, if and when approved, by patients, the medical community and third-party payors, competing effectively with other therapies, and obtaining and maintaining coverage and adequate reimbursement from third-party payors;
- maintaining a continued acceptable safety profile of our products following approval; and
- protecting our intellectual property rights, including obtaining and maintaining patent and trade secret protection and regulatory exclusivity.

In certain cases, such as in our ongoing collaboration with AffaMed, many of these factors may be or are beyond our control, including clinical development and sales, marketing and distribution efforts. If we or our collaborators do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our products and product candidates, which would materially harm our business.

Even though DEXTENZA has received marketing approval from the FDA and even if any of our product candidates receives marketing approval, these products may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success, and the market opportunity for these products may be smaller than we estimate.

DEXTENZA, ReSure Sealant or any of our product candidates that receives marketing approval may fail to gain market acceptance by physicians, patients, third-party payors and others in the medical community. We commercially launched ReSure Sealant in the first quarter of 2014, DEXTENZA for the treatment of post-surgical ocular inflammation and pain in July 2019, and DEXTENZA for the treatment of ocular itching associated with allergic conjunctivitis in the first quarter of 2022, and we cannot yet accurately predict the extent to which these products will gain market acceptance and become commercially successful, if at all.

The degree of market acceptance of any of our products, or any product candidate for which we obtain marketing approval will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments;
- our ability to offer our products for sale at competitive prices, particularly in light of the lower cost of alternative treatments;
- the clinical indications for which the product is approved;
- the convenience and ease of administration compared to alternative treatments, including the intracanalicular insert retention rate for our intracanalicular insert products and product candidates;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of our marketing and distribution support;
- timing of market introduction of competitive products;
- the availability of third-party coverage and adequate reimbursement;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our products together with other medications.

For example, because we have not conducted any clinical trials to date comparing the effectiveness of DEXTENZA directly to currently approved alternative treatments for post-surgical ocular inflammation and pain following cataract surgery or ocular itching associated with allergic conjunctivitis, market acceptance of DEXTENZA could be less than if we had conducted such trials, and we may not be able to achieve the market share we anticipate.

Our assessment of the potential market opportunity for DEXTENZA and 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. 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. If the actual market for DEXTENZA or any of our product candidates is smaller than we expect, our product revenue may be limited and it may be more difficult for us to achieve or maintain profitability.

If we are unable to establish and maintain adequate sales, marketing and distribution capabilities, we may not be successful in commercializing DEXTENZA or any product candidates if and when they are approved.

We have limited experience in the sale, marketing and distribution of drug and device products. To achieve commercial success for DEXTENZA and any product candidate for which we obtain marketing approval, we will need to establish and maintain adequate sales, marketing and distribution capabilities, either ourselves or through collaborations or other arrangements with third parties. We have built our own highly targeted, key account sales force for DEXTENZA that has focused primarily on ambulatory surgical centers, or ASCs, responsible for the largest volumes of cataract surgery.

We believe that certain of our product candidates, if they are successfully developed and obtain marketing approval, would be used in ophthalmologists' offices, similar to DEXTENZA for the treatment of allergic conjunctivitis. We believe the office setting offers a unique set of potential challenges. If we do not succeed in adapting our marketing efforts to include the office setting, our ability to commercialize DEXTENZA to its fullest potential or any future product candidates used in the office setting would be adversely affected.

Because we have not historically evaluated whether to seek regulatory approval for any of our products or product candidates outside of the United States, pending potential receipt of regulatory approval for the applicable product candidate in the United States, at this time we cannot be certain when, if ever, we will recognize revenue from commercialization of our products or product candidates in any international markets. If we decide to commercialize our products outside of the United States, we expect to utilize a variety of types of collaboration, distribution and other marketing arrangements with one or more third parties to commercialize any product of ours that receives marketing approval. These may include independent distributors, pharmaceutical companies or our own direct sales organization. For example, we intend to rely on AffaMed to commercialize DEXTENZA and PAXTRAVA, if approved for marketing, in specified jurisdictions in Asia in connection with our collaboration agreement with AffaMed.

There are risks involved with both establishing our own sales, marketing and distribution capabilities and with entering into arrangements with third parties to perform these services. We may not be successful in entering into arrangements with third parties to sell, market and distribute our products or may be unable to do so on terms that are most beneficial to us. Such third parties may have interests that differ from ours. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to market, sell and distribute our products effectively. Our product revenues and our profitability, if any, under third-party collaboration, distribution or other marketing arrangements may also be lower than if we were to sell, market and distribute a product ourselves. On the other hand, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of any product or product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Other factors that may inhibit our efforts to commercialize products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or lack of adequate number of physicians to use or prescribe our products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we do not establish and maintain sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing DEXTENZA or any of our product candidates.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new drug and device products is highly competitive. We face competition with respect to our products and product candidates, and will face competition with respect to any other product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

Our products and product candidates target markets that are already served by a variety of competing products based on a number of active pharmaceutical ingredients. Many of these existing products have achieved widespread acceptance among physicians, patients and payors for the treatment of ophthalmic diseases and conditions. In addition, many of these products are available on a generic basis, and our products and product candidates may not demonstrate sufficient additional clinical benefits to physicians, patients or payors to justify a higher price compared to generic products. In many cases, insurers or other third-party payors, particularly Medicare, encourage the use of generic products. As a result, our products face, and product candidates, if approved, will face, competition from drugs based on the same or similar active pharmaceutical ingredients but that are administered in a different manner, typically through eye drops or intravitreal injections.

Because the active pharmaceutical ingredients in our products and product candidates are primarily available on a generic basis, or are soon to be available on a generic basis, competitors will be able to offer and sell products with the same active pharmaceutical ingredient as our products so long as these competitors do not infringe the patents that we license or own. For example, our licensed patents related to our intracanalicular insert products and product candidates largely relate to the hydrogel composition of the intracanalicular inserts and certain drug-release features of the inserts. As such, if a third party were able to design around the formulation and process patents that we license or own and create a different formulation using a different production process not covered by our licensed patents or patent applications, we would likely be unable to prevent that third party from manufacturing and marketing its product.

Other companies have advanced into Phase 3 clinical development biodegradable, programmed-release drug delivery product candidates that could compete with our intracanalicular insert products and product candidates. Multiple companies are exploring in early-stage development alternative means to deliver anti-VEGF and TKI products in an extended-delivery fashion to the back of the eye. There are also multiple branded, generic and over-the-counter products, in the dry eye space, including Restasis, for increasing tear production, marketed by Allergan; Cequa for increasing tear production, marketed by Sun Ophthalmics in the United States; lifitegrast, for the treatment of the signs and symptoms of dry eye disease, marketed by Bausch & Lomb (previously marketed by Novartis) under the brand name Xiidra®; and off-label use of corticosteroids.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, are less expensive than our products or have better reimbursement. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific, manufacturing, marketing, and management personnel, establishing clinical trial sites and subject registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

DEXTENZA and any product candidates for which we obtain marketing approval may become subject to unfavorable pricing regulations, third-party coverage or reimbursement practices or healthcare reform initiatives, which could harm our business.

Our ability to commercialize DEXTENZA or any product candidates that we may develop successfully will depend, in part, on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government healthcare programs, private health insurers, managed care plans and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug and device companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Coverage and reimbursement may not be available for DEXTENZA or any other product that we commercialize and, even if they are available, the level of reimbursement may not be satisfactory.

Inadequate reimbursement may adversely affect the demand for, or the price of, DEXTENZA or any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize DEXTENZA or any product candidates for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs and devices, and coverage may be more limited than the indications for which the drug is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any FDA-approved products that we develop would compromise our ability to generate revenues and become profitable.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug and device products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product or product candidate to other available therapies. Adverse pricing limitations may hinder our ability to recoup our investment in one or more products or product candidates, even if our product candidates obtain marketing approval.

DEXTENZA or any product candidate for which we obtain marketing approval in the United States or in other countries may not be considered medically reasonable and necessary for a specific indication, may not be considered cost-effective by third-party payors, coverage and an adequate level of reimbursement may not be available, and reimbursement policies of third-party payors may adversely affect our ability to sell our products and product candidates profitably. DEXTENZA is currently considered a post-surgical product, in the same fashion as eye drops. However, if

DEXTENZA were instead categorized as an intra-operative product, it would not be subject to separate reimbursement in ASCs and hospital out-patient departments, or HOPDs, which could likewise limit its market acceptance.

A specific and permanent J-Code for ophthalmic inserts containing dexamethasone including DEXTENZA is in effect, and DEXTENZA currently benefits from separate payment in the ASC setting because it meets the criteria set forth for non-opioid pain management drugs as a surgical supply provision. CMS evaluates the eligibility of products such as DEXTENZA for separate payment annually, and there can be no assurance that CMS will not change the criteria applicable to non-opioid pain management drugs for 2024 or beyond. If DEXTENZA is no longer eligible for reimbursement separately from ophthalmic surgery in the ASC setting, due to the loss of pass-through status or otherwise, our net product revenues, which currently consist primarily of DEXTENZA sales in reliance on separate reimbursement through pass-through status, would decline significantly, and our ability to generate revenues from future sales of DEXTENZA for the treatment of post-surgical ocular inflammation and pain would be adversely affected.

CMS has also established the fixed reimbursement amount for Category I Current Procedural Terminology, or CPT, code 68841, the procedure code for the insertion of DEXTENZA. As this fee schedule is lower than reimbursement many physicians received under the prior Category III CPT code for DEXTENZA, physicians may have less incentive to use DEXTENZA and, as a result, our ability to continue to commercialize DEXTENZA may decrease. Additionally, CMS will review such determination as part of its annual rulemaking cycle, and such amount could be further reduced in the future. Physicians' desire to use DEXTENZA could also be adversely impacted if competitive products secure higher procedure payments for their use than DEXTENZA.

There are no assurances that we will be successful in maintaining reimbursement for DEXTENZA or of obtaining or maintaining reimbursement for any products or product candidates for which we might receive marketing approval in the future.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we develop.

We face an inherent risk of product liability exposure related to the use of our product candidates that we develop in human clinical trials. We face an even greater risk for any products we develop and commercially sell or have sold, including DEXTENZA and ReSure Sealant. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any products or product candidates that we develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or subjects;
- loss of revenue;
- reduced time and attention of our management to pursue our business strategy; and
- the inability to commercialize any products that we develop.

We currently hold product liability insurance coverage; however these policies may not be adequate to cover all liabilities that we may incur and we may need to increase our insurance coverage as we expand our clinical trials and our sales of DEXTENZA and any product candidates for which we obtain marketing approval. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks Related to Manufacturing

If our sole clinical and commercial manufacturing facility is damaged or destroyed or production at this facility is otherwise interrupted, our business and prospects would be negatively affected.

If our single-site manufacturing facility or the equipment in it is damaged or destroyed, we may not be able to quickly or inexpensively replace our manufacturing capacity or replace it at all. In the event of a temporary or protracted loss of this facility or equipment, we might not be able to transfer manufacturing to another facility or to a third party. Even if we could transfer our manufacturing to another facility or a third party, the shift would likely be expensive and time-consuming, particularly since any new facility would need to comply with the necessary regulatory requirements and to be inspected and qualified. We would also need FDA approval before any products manufactured at that facility could be used for commercial supply. In the case of any disruption in our manufacturing operations at this facility, we may not have sufficient quantities of our product candidates to meet our clinical trial requirements or of our product inventory to meet our commercial requirements. Such an event could delay our clinical trials or, particularly because we have sought to adopt just-in-time manufacturing practices and maintain limited commercial product inventory with our distributors, reduce our product sales.

Currently, we maintain insurance coverage against damage to our property and equipment and to cover business interruption and research and development restoration expenses. However, our insurance coverage may not reimburse us, or may not be sufficient to reimburse us, for any expenses or losses we may suffer. We may be unable to meet our requirements for DEXTENZA or any of our product candidates if there were a catastrophic event or failure of our current manufacturing facility or processes.

We will need to upgrade and expand our manufacturing facility or relocate to another facility and to augment our manufacturing personnel and processes in order to meet our business plans. If we fail to do so, we may not have sufficient quantities of our products or product candidates to meet our commercial and clinical trial requirements.

We manufacture DEXTENZA and our product candidates for use in clinical trials, research and development and commercial efforts at our single-site clinical and commercial manufacturing facility located in Bedford, Massachusetts. In order to meet our business plan, which contemplates our scaling up manufacturing processes to support the commercialization of our current products and the development and potential commercialization of our current and future product candidates, we will need to upgrade and expand our existing manufacturing facility, or relocate to another manufacturing facility; add manufacturing, quality and support personnel; ensure that new processes, systems, and facilities are qualified and validated; and ensure that any new processes and systems are consistently implemented in our facility or facilities. The upgrade and expansion of our facility, or the relocation to an additional facility, will require additional regulatory approvals including FDA audits of such new processes, systems, and facilities. In addition, it will be costly and time-consuming to expand our facility or relocate to another facility and recruit necessary additional personnel. If we are unable to expand our manufacturing facility or relocate to another facility in compliance with regulatory requirements or to hire additional necessary manufacturing personnel, we may encounter delays or additional costs in achieving our research, development and commercialization objectives, including obtaining regulatory approvals of our product candidates and meeting customer demand for our products, which could materially damage our business and financial position.

We must comply with federal, state and foreign regulations, including quality standards applicable to medical device and pharmaceutical manufacturers, such as cGMP, which are enforced by the FDA through means including its facilities inspection program and system audits and by similar regulatory authorities in other jurisdictions where we do business. These requirements include, among other things, quality control, quality systems and the maintenance of records and documentation. For example, between March 2015 and May 2018, we received multiple Form 483s from the FDA containing inspectional observations relating to inadequate procedures for documenting follow-up information pertinent to the investigation of complaints and for evaluation of complaints for adverse event reporting; process controls, analytical testing and physical security procedures related to manufacture of our drug product for stability and commercial production purposes; and procedures for manufacturing processes and analytical testing related to the manufacture of drug product for commercial production. In each of July 2016 and July 2017, we also received a Complete Response Letter, or CRL, from the FDA regarding our NDA for DEXTENZA pertaining to, among other things, the deficiencies in manufacturing processes, controls, and analytical testing identified during pre-NDA approval inspections of our manufacturing facility documented on Form 483s. We may be subject to similar inspections, audits and other requirements in connection with subsequent applications for other product candidates or in connection with periodic, routine surveillance for products for which we have received marketing authorization.

The FDA or similar foreign regulatory authorities at any time also may implement new standards, or change their interpretation and enforcement of existing standards, for the manufacture, packaging or testing of our products. Any failure to comply with applicable regulations may result in fines and civil penalties, suspension of production, product seizure or recall, imposition of a consent decree, or withdrawal of product approval, and would limit the availability of DEXTENZA and our product candidates that we manufacture.

Any manufacturing defect or error discovered after products have been produced and distributed could result in significant consequences, including costly recall procedures, re-stocking costs, damage to our reputation and potential for product liability claims.

We expect to continue to contract with third parties for at least some aspects of the production of our products and product candidates. We also depend from time to time on single-source suppliers for certain materials used in the manufacturing of our products and product candidates. This increases the risk that we will not have sufficient quantities of our products or product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We currently rely on third parties for some aspects of the production of DEXTENZA and our product candidates for commercialization and preclinical testing and clinical trials. While we expect that our existing manufacturing facility, or additional facilities that we might build, will be sufficient to meet our requirements for manufacturing DEXTENZA and any of our product candidates for which we obtain marketing approval, we may in the future need to rely on third-party manufacturers for some aspects of the manufacture of our products or product candidates.

We also depend on single-source suppliers for certain materials used in the manufacturing of our products and product candidates, including our supply of PEG, the molecule that forms the basis of our hydrogels, and other raw materials of our products and product candidates and for sterilization and packaging of the finished product. We do not have any long-term supply agreements in place for the clinical or commercial supply of any drug substances or raw materials for DEXTENZA or any of our product candidates. We purchase drug substance and raw materials, including the chemical constituents for our hydrogel, from independent suppliers on a purchase order basis. We cannot ensure that our suppliers will remain in business, have sufficient capacity or supply to meet our needs or that they will not be purchased by one of our competitors or another company that is not interested in continuing to work with us. Our use of single-source suppliers of raw materials and other components used in the manufacturing of our products and product candidates could expose us to several risks, including disruptions in supply, price increases or late deliveries. Any performance failure or refusal to supply drug substance or raw materials on the part of our existing or future suppliers could delay clinical development, marketing approval or commercialization of our products. If our current suppliers do not perform as we expect, we may be required to replace one or more of these suppliers. Establishing additional or replacement suppliers could take a substantial amount of time, and it may be difficult to establish replacement suppliers who meet our quality standards and applicable regulatory requirements. For example, we depend on a sole source supplier for the supply of our PEG. This sole source supplier may be unwilling or unable to supply PEG to us reliably, continuously and at the levels we anticipate or are required by the market. Although we believe that there are a number of potential long-term replacements to our suppliers, including our PEG supplier, we may incur added costs and delays in identifying and qualifying any such replacements.

Reliance on third parties for aspects of the supply of our products and product candidates entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how;
- the possible breach of an agreement by the third party; and
- the possible termination or nonrenewal of an agreement by the third party at a time that is costly or inconvenient for us.

Third-party suppliers or manufacturers may not be able to comply with our specifications, quality assurance standards, cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third parties, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products and product candidates. Further, reliance on third-party suppliers or manufacturers may adversely affect our future profit margins and our ability to commercialize any products that receive regulatory approval on a timely and competitive basis.

Risks Related to Our Dependence on Third Parties

We have entered into collaborations with third parties to develop certain product candidates, and in the future we may enter into additional collaborations for the development or commercialization of our product candidates. We may also enter into collaboration, distribution or marketing arrangements for the commercialization of DEXTENZA, ReSure Sealant, or any product candidates for which we obtain marketing approval. If our collaborations are not successful, we may not be able to capitalize on the market potential of these products or product candidates.

We have in the past entered into collaboration agreements with third parties, including our collaboration with AffaMed, and expect to utilize a variety of types of collaboration, distribution and other marketing arrangements with third parties to commercialize DEXTENZA, or any of our product candidates for which we obtain marketing approval in markets outside the United States. We also may enter into arrangements with third parties to perform these services in the United States if we do not establish our own sales, marketing and distribution capabilities in the United States for such products or if we determine that such third-party arrangements are otherwise beneficial. We also may seek additional third-party collaborators for development and commercialization of product candidates, including PAXTRAVA and AXPAXLI. Our likely collaborators for any sales, marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements.

Our collaboration with AffaMed poses, and any future collaborations likely will pose, a number of risks including the following:

- collaborators have significant discretion in determining the amount and timing of efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of our products or product candidates that receive marketing approval or may elect not to continue or renew development or commercialization programs based on results of clinical trials or other studies, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could be subject to bankruptcy proceedings or other similar arrangements which may result in us having to return funds that we previously received, or in collaborators selling or transferring product licenses to other parties;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;

- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;

- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;

- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of products or product candidates, might lead to additional responsibilities for us with respect to products or product candidates, or might result in litigation or arbitration, any of which would divert management attention and resources, be time-consuming and expensive;

- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;

- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and

- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable products or product candidates.

Collaboration agreements may not lead to the development or commercialization of products or product candidates in the most efficient manner, or at all. If any collaborations that we enter into do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, or if we are required to return previously received funds, or if product licenses are sold or transferred to another party as a result of a collaborators' bankruptcy, our development of our products or product candidates could be delayed and we may need additional resources to develop our products or product candidates. For example, our former collaborator Regeneron terminated our collaboration in August 2021. As a result of the termination, we were relieved of obligations to reimburse Regeneron for certain development costs, up to an aggregate amount of $30.0 million in certain circumstances, were Regeneron to exercise its option but also ceased to be eligible to receive (i) reimbursement from Regeneron for ongoing research and development activities, (ii) a fee upon exercise of its option, (iii) payments upon the achievement of specified development and regulatory milestones of the products developed under the collaboration, or (iv) tiered, escalating royalties on such products. All of the risks relating to product development, regulatory approval and commercialization described in this periodic report also apply to the activities of our collaborators.

Additionally, if one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be harmed.

If we are not able to establish additional collaborations, we may have to alter our development and commercialization plans and our business could be adversely affected.

In October 2020, we entered into a collaboration with AffaMed for the development and commercialization of DEXTENZA regarding ocular inflammation and pain following cataract surgery and ocular itching associated with allergic conjunctivitis and for PAXTRAVA regarding OAG and OHT in specified territories in Asia. For some of our product candidates, we may decide to collaborate with pharmaceutical, biotechnology and medical device companies for the development and commercialization of one or more of our product candidates. We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to subjects, the potential of competing products, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under current or future license and collaboration agreements from entering into agreements on certain terms with potential collaborators. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. If we are unable to reach agreements with suitable collaborators on a timely basis and on acceptable terms, we may have to curtail the development of a product candidate, reduce or delay one or more development programs, or limit potential commercialization activities. If we elect to fund and undertake development or commercialization activities on our own, we will need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our product platform.

Although the majority of our clinical development is administered and managed by our own employees, we have relied, and may continue to rely, on third parties for certain aspects of our clinical development, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

Our employees have administered and managed most of our clinical development work to date. However, we also utilize third parties, such as CROs, to conduct clinical trials of certain of our product candidates, including AXPAXLI for the treatment of wet AMD and NPDR and PAXTRAVA for the treatment of OAG or OHT, and we may continue to do so. If we deem necessary, we may engage additional third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct or assist in our clinical trials or other clinical development work. If we are unable to enter into an agreement with a CRO or other service provider when required, our product development activities could be delayed.

Our reliance on third parties for research and development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials, including the SOL-1 trial and the HELIOS trial, is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as good clinical practices for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected, even if a third party is administering certain activities. For example, in May 2020, we disclosed the receipt of interim data regarding our Phase 1 clinical trial of AXPAXLI, in Australia, for the treatment of wet AMD and other retinal diseases. We discovered, however, that our disclosures did not include complete information when we became aware in July 2020 that a clinical trial site had not entered certain data concerning these subjects into the clinical trial database in a timely manner. If we engage third parties and they do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

Risks Related to Our Intellectual Property

We may be unable to obtain and maintain patent protection for our technology and products, or the scope of the patent protection obtained may not be sufficiently broad, such that our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be impaired.

Our success depends in large part on our and our licensor's ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology and products. We and our licensor have sought to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies, products and product candidates. Our licensed and owned patent portfolio that we believe is integral to our business includes patents with terms that extend from 2024 to 2041. Given the amount of time required for the development, testing and regulatory review of new product candidates, we may have a reduced patent exclusivity period upon approval. The patent prosecution process is expensive and time-consuming, and we may not have filed or prosecuted and may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we have failed, or may in the future fail, to identify patentable aspects of our research and development efforts before it is too late to obtain patent protection.

In some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to enforce or maintain the patents, covering technology that we license from third parties. In particular, the license agreement that we have entered into with Incept LLC, or Incept, an intellectual property holding company, which covers a significant portion of the patent rights and the technology for DEXTENZA, ReSure Sealant and our product candidates, provides that, with limited exceptions, Incept has sole control and responsibility for ongoing prosecution for certain patents covered by the license agreement. In addition, although we have a right under the Incept license to bring suit against third parties who infringe such licensed patents in our fields, other Incept licensees may also have the right to enforce these patents in their own respective fields without our oversight or control. Those other licensees may choose to enforce our licensed patents in a way that harms our interest, for example, by advocating for claim interpretations or agreeing on invalidity positions that conflict with our positions or our interest. For example, three of our licensed patents related to ReSure Sealant were invalidated and rendered unenforceable following their assertion by Integra LifeSciences Holdings Corporation, another licensee of Incept. We also have no right to control the defense of such licensed patents if their validity or scope is challenged before the U.S. Patent and Trademark Office, or USPTO, or other patent office or tribunal. Instead, we would essentially rely on our licensor to defend such challenges, and it may not do so in a way that would best protect our interests. Therefore, certain of our licensed patents and applications may not be prosecuted, enforced, defended or maintained in a manner consistent with the best interests of our business. If Incept fails to prosecute, enforce or maintain such patents, or loses rights to those patents, our licensed patent portfolio may be reduced or eliminated.

The patent position of pharmaceutical, biotechnology and medical device companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights, including our licensed patent rights, are highly uncertain. Our and our licensor’s pending and future patent applications may not result in patents being issued which protect our technology or products or which effectively prevent others from commercializing competitive technologies and products. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Patents might not be issued and we may never obtain any patent protection or may only obtain substantially limited patent protection outside of the United States with respect to our products. Further, the complexity and uncertainty of European patent laws have increased in recent years. In Europe, a new unitary patent system will likely be introduced by the end of 2023, which would significantly impact European patents, including those granted before the introduction of such a system. Under the unitary patent system, European applications will soon have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the Unitary Patent Court (UPC). As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation. Patents granted before the implementation of the UPC will have the option of opting out of the jurisdiction of the UPC and remaining as national patents in the UPC countries. Patents that remain under the jurisdiction of the UPC will be potentially vulnerable to a single UPC-based revocation challenge that, if successful, could invalidate the patent in all countries who are signatories to the UPC. We cannot predict with certainty the long-term effects of any potential changes.

Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we or our licensor were the first to make the inventions claimed in our licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions. Databases for patents and publications, and methods for searching them, are inherently limited so it is not practical to review and know the full scope of all issued and pending patent applications. As a result, the issuance, scope, validity, enforceability and commercial value of our licensed and owned patent rights are uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Moreover, changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. The Leahy-Smith America Invents Act, or the Leahy-Smith Act, includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The USPTO developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. The first to file provisions limit the rights of an inventor to patent an invention if not the first to file an application for patenting that invention, even if such invention was the first invention. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act 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. For example, the Leahy-Smith Act provides an administrative tribunal known as the Patent Trial and Appeals Board, or PTAB, that provides a venue for companies to challenge the validity of competitor patents at a cost that is much lower than district court litigation and on timelines that are much faster. Although it is not clear what, if any, long term impact the PTAB proceedings will have on the operation of our business, the results of patent challenge proceedings before the PTAB since its inception in 2013 have resulted in the invalidation of many U.S. patent claims. The availability of the PTAB as a lower-cost, faster and potentially more potent tribunal for challenging patents could therefore increase the likelihood that our own licensed and owned patents will be challenged, thereby increasing the uncertainties and costs of maintaining and enforcing them. Moreover, if such challenges occur, as indicated above, we have no right to control the defense of our licensed portfolio. Instead, we would essentially rely on our licensor to consider our suggestions and to defend such challenges, with the possibility that it may not do so in a way that best protects our interests.

We may be subject to a third-party preissuance submission of prior art to the USPTO, or become involved in other contested proceedings such as opposition, derivation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future products.

In the United States, the FDA does not prohibit physicians from prescribing an approved product for uses that are not described in the product’s labeling. Although use of a product directed by off-label prescriptions may infringe our method-of-treatment patents, the practice is common across medical specialties, particularly in the United States, and such infringement is difficult to detect, prevent or prosecute. In addition, patents that cover methods of use for a medical device cannot be enforced against the party that uses the device, but rather only against the party that makes them. Such indirect enforcement is more difficult to achieve.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our licensed and owned patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products.

Because the active pharmaceutical ingredients in our products and product candidates are primarily available on a generic basis, or are soon to be available on a generic basis, competitors will be able to offer and sell products with the same active pharmaceutical ingredient as our products so long as these competitors do not infringe our patents or any patents that we license. These patents largely relate to the hydrogel composition and drug-release design scheme of our products. As such, if a third party were able to design around the formulation and process patents that we license and own and create a different formulation using a different production process not covered by our patents or patent applications, we would likely be unable to prevent that third party from manufacturing and marketing its product.

If we are not able to obtain patent term extensions in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation, thereby potentially extending the term of our marketing exclusivity for our product and product candidates, our business may be impaired.

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one of the U.S. patents covering each of such product candidates or the use thereof may be eligible for up to five years of patent term restoration under the Hatch-Waxman Act. The Hatch-Waxman Act allows a maximum of one patent to be extended per FDA-approved product. Patent term extension also may be available in certain foreign countries upon regulatory approval of our product candidates. Nevertheless, we may not be granted patent term extension either in the United States or in any foreign country because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request.

Further, our license from Incept does not provide us with the right to control decisions by Incept or its other licensees on Orange Book listings or patent term extension decisions under the Hatch-Waxman Act. Thus, if one of our important licensed patents is eligible for a patent term extension under the Hatch-Waxman Act, and it covers a product of another Incept licensee in addition to our own product candidate, we may not be able to obtain that extension if the other licensee seeks and obtains that extension first.

If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product may be shortened and our competitors may obtain approval of competing products following our patent expiration sooner, and our revenue could be reduced, possibly materially.

We may become involved in lawsuits to protect or enforce our licensed and owned patents or other intellectual property, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our licensed or owned patents or other intellectual property. As a result, to counter infringement or unauthorized use, we may file infringement claims, which can be expensive and time-consuming. Under the terms of our license agreement with Incept, we have the right to initiate suit against third parties who we believe infringe on the patents subject to the license. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent we have rights to is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability to develop, manufacture, market and sell our products and product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. We may become party to, or threatened with, infringement litigation claims regarding our products and technology, including claims from competitors or from non-practicing entities that have no relevant product revenue and against whom our own patent portfolio may have no deterrent effect. Moreover, we may become party to future adversarial proceedings or litigation regarding our patent portfolio or the patents of third parties. Such proceedings could also include contested post-grant proceedings such as oppositions, *inter partes* review, reexamination, interference or derivation proceedings before the USPTO or foreign patent offices. The legal threshold for initiating litigation or contested proceedings is low, so that even lawsuits or proceedings with a low probability of success might be initiated and require significant resources to defend. Litigation and contested proceedings can also be expensive and time-consuming, and our adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we or our licensor can. The risks of being involved in such litigation and proceedings may increase as our products or product candidates near commercialization and as we gain the greater visibility associated with being a public company. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. We may not be aware of all such intellectual property rights potentially relating to our products or product candidates and their uses, or we may incorrectly determine that a patent is invalid or does not cover a particular product or product candidate. Thus, we do not know with certainty that any of our products or product candidates, or our commercialization thereof, does not and will not infringe or otherwise violate any third party's intellectual property.

We have been made aware by a third party of patents relating to intracanalicular inserts that may relate to, and potentially could be asserted against, our intracanalicular insert product and product candidates, including DEXTENZA.

We believe that DEXTENZA does not infringe any claims of these patents. We also believe that such claims, if and to the extent they were asserted against our product candidates, would be subject to claims of invalidity. We initiated legal proceedings against one of these patents and administrative proceedings against the other two patents in order to show that DEXTENZA does not infringe the claims of these patents or that these patents are invalid. Legal proceedings related to one of these patents has been dismissed by agreement of the parties without prejudice. The USPTO decided to proceed with the administrative proceeding related to one of the patents while declining to do so for the other after determining that we had not established a reasonable likelihood that we would prevail in establishing the unpatentability of certain claims. In June 2020, for the patent for which the USPTO decided to proceed with administrative proceedings, the PTAB, after an *inter partes* review, determined that we had proven by a preponderance of the evidence that all claims of the patent at issue held by such third party were invalid. The third party appealed this decision, and in November 2021, the United States Court of Appeals for the Federal Circuit affirmed the holding of the PTAB. The period during which such third party may appeal the decision of the Court of Appeals has lapsed. We continue to believe that DEXTENZA does not infringe the claims of these patents and that, if and to the extent it were asserted against DEXTENZA, such patent would be subject to a claim of invalidity. We have become aware that the USPTO has recently issued a patent filed by this third party related to intracanalicular inserts containing dexamethasone. If this patent were asserted against DEXTENZA or other of our product candidates, we believe such patent would be non-infringed and subject to a claim of invalidity.

If we are found to infringe a third party's intellectual property rights, we could be required to cease manufacturing or commercializing the infringing product or product candidate or to obtain a license from such third party to continue developing and marketing our products and product candidates. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product containing such technology. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent and could be forced to indemnify our customers or collaborators. A finding of infringement could also result in an injunction that prevents us from commercializing our products or product candidates or forces us to cease some of our business operations. In addition, we may be forced to redesign our products or product candidates, seek new regulatory approvals thereby causing delays, and indemnify third parties pursuant to contractual agreements. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

If we fail to comply with our obligations in our intellectual property licenses and funding arrangements with third parties, we could lose rights that are important to our business.

Our license agreement with Incept, under which we license certain portions of our patent rights and the technology for our products and product candidates, imposes royalty and other financial obligations and other substantial performance obligations on us. We also may enter into additional licensing and funding arrangements with third parties that may impose diligence, development and commercialization timelines and milestone payment, royalty, insurance and other obligations on us. If we fail to comply with our obligations under current or future license and collaboration agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to manufacture or market any product that is covered by these agreements or may face other penalties under the agreements. Such an occurrence could diminish the value of our product. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

Under the terms of our license agreement with Incept, we have agreed to assign to Incept our rights in certain patent applications filed at any time in any country for which one or more inventors are under an obligation of assignment to us. These assigned patent applications and any resulting patents are included within the specified patents owned or controlled by Incept to which we receive a license under the agreement. Incept has retained rights to practice the patents and technology licensed to us under the agreement for all purposes other than for researching, designing, developing, manufacturing and commercializing products that are delivered to or around the human eye for diagnostic, therapeutic or prophylactic purposes relating to ophthalmic diseases or conditions. As a result, termination of our agreement with Incept, based on our failure to comply with this or any other obligation under the agreement, would cause us to lose a significant portion of our rights to important intellectual property or technology upon which our business depends. Additionally, the field limit of the license and the requirement that we assign to Incept our rights in certain patent applications may restrict our ability to use certain of our licensed rights to expand our business outside of the specified fields. If we determine to pursue a strategy of expanding the use of the hydrogel technology outside of the specified fields, we would need to negotiate and enter into an amendment to our existing license agreement with Incept or a new license agreement with Incept covering one or more additional such fields of use or utilize technologies that do not infringe on such licensed rights. We may not be able to obtain any such required amendment or new license or to invent or otherwise access other technology on commercially reasonable terms or at all.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other biotechnology, medical device or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these employees or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own, such agreements may be ineffective, or such agreements may be breached by our counterparty.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for our technology, products and product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

If the FDA or comparable foreign regulatory authorities approve generic versions of our current commercial product or any of our future drug products that receive marketing approval through the NDA pathway, or such authorities do not grant such future products appropriate periods of data exclusivity before approving generic versions of our products, our sales could be adversely affected.

Once an NDA is approved, the product covered thereby becomes a "reference-listed drug" in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly known as the Orange Book. Manufacturers may seek approval of generic versions of reference-listed drugs through submission of abbreviated new drug applications, or ANDAs, in the United States. In support of an ANDA, a generic manufacturer need not conduct clinical trials to assess safety and efficacy. Rather, the applicant generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labeling as the reference-listed drug and that the generic version is bioequivalent to the reference-listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference-listed drug and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference-listed drug is typically lost to the generic product.

The FDA may not approve an ANDA for a generic product until any applicable period of non-patent exclusivity for the reference-listed drug has expired. The Federal Food, Drug, and Cosmetic Act, or FDCA, provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity, or NCE. For the purposes of this provision, an NCE is a drug that contains an active moiety that has previously been approved by the FDA in any other NDA. This interpretation was confirmed with enactment of the Ensuring Innovation Act in April 2021. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. Specifically, in cases where such exclusivity has been granted, an ANDA may not be submitted to the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference-listed drug is either invalid or will not be infringed by the generic product, in which case the applicant may submit its application four years following approval of the reference-listed drug. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical trials, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application.

Generic drug manufacturers may seek to launch generic products following the expiration of any applicable exclusivity period we obtain if our product candidates are approved, even if we still have patent protection for such product candidates. Competition that any such product candidates of ours may face from generic versions of such products could materially and adversely impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we may make in those product candidates.

Risks Related to Regulatory Approval and Marketing of Our Product Candidates and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the regulatory approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we or any current or future collaborator of ours is not able to obtain, or if there are delays in obtaining, required regulatory approvals, we or they will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

The activities associated with the development and commercialization of our products and product candidates, including design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities in the United States and by the EMA and similar regulatory authorities outside the United States. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have only received approval to market DEXTENZA and ReSure Sealant in the United States, and have not received approval to market any of our product candidates or to market DEXTENZA or ReSure Sealant in any jurisdiction outside the United States. Further, we have only received approval to market DEXTENZA for the treatment of ocular inflammation and pain following ophthalmic surgery and ocular itching associated with allergic conjunctivitis. If we are unable to obtain a CE Certificate of Conformity for any of our products or product candidates for which we seek European regulatory approval, we will be prohibited from commercializing such product or products in the European Union and other places which require the CE Certificate of Conformity. In such a case, the potential market to commercialize our products may be significantly smaller than we currently estimate.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive and may take many years, if approval is obtained at all. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and purity. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. The FDA, the EMA or other regulatory authorities may determine that our product candidates are not safe or effective, are only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use.

As part of its review of the NDA for DEXTENZA for post-surgical ocular pain, the FDA completed inspections of three sites from our two completed Phase 3 clinical trials for compliance with the study protocol and Good Clinical Practices as well as two inspections of our manufacturing facility. The FDA identified several deficiencies and issued us multiple Forms 483s and two CRLs, each of which delayed our development and commercialization efforts. We may be subject to similar inspections in the future for any of our products and product candidates.

Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA, the EMA and regulatory authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we or any current or future collaborator of ours ultimately obtains may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Accordingly, if we or any current or future collaborator of ours experiences delays in obtaining approval or if we or they fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

Even if we, or any current or future collaborators, obtain marketing approvals for our product candidates, the terms of approvals, ongoing regulations and post-marketing restrictions for our products may limit how we manufacture and market our products, which could materially impair our ability to generate revenue.

Once marketing approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation.

Manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs applicable to drug and biologic manufacturers or quality assurance standards applicable to medical device manufacturers, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, any contract manufacturers we may engage in the future, our current or future collaborators and their contract manufacturers will also be subject to other regulatory requirements, including submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements regarding the distribution of samples to physicians, recordkeeping, and costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product such as the requirement to implement a risk evaluation and mitigation strategy.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses 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 candidate. For example, the FDA required two post-approval studies as a condition for approval of our premarket approval application for ReSure Sealant, the last of which the FDA confirmed was complete in April 2021. The studies were expensive, required extensive communication and coordination with the FDA, and took more than five years to complete. The FDA also has required us to conduct a clinical trial of DEXTENZA for the treatment of post-surgical ocular inflammation and pain and for the treatment of ocular itching associated with allergic conjunctivitis in pediatric populations in accordance with the Pediatric Research Equity Act of 2003.

Certain endpoint data we hope to include in any approved product labeling also may not make it into such labeling, including exploratory or secondary endpoint data such as patient-reported outcome measures. The FDA may also require a Risk Evaluation and Mitigation Strategy, or REMS, program as a condition of approval of our product candidates, which could entail requirements for long-term patient follow-up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA, EMA or a comparable non-U.S. regulatory authority approves our product candidates, we will have to comply with requirements including submissions of safety and other post-marketing information and reports and registration.

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

- restrictions on the marketing or manufacturing of our products, 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 license approvals;
- product seizure or detention or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

In addition, we are, or may become, subject to various U.S. federal, state, and local laws, regulations, and recommendations relating to safe working conditions, laboratory and manufacturing practices, the experimental use of animals, and the use and disposal of hazardous substances, including radioactive compounds and infectious disease agents, used in connection with our research work. If we fail to comply with the laws and regulations pertaining to our business, we may be subject to sanctions, including the temporary or permanent suspension of operations, product recalls, marketing restrictions, and civil and criminal penalties.

Finally, our ability to develop and market new drug products may be impacted by ongoing litigation challenging the FDA's approval of mifepristone. Specifically, on April 7, 2023, the U.S. District Court for the Northern District of Texas stayed the approval by the FDA of mifepristone, a drug product which was originally approved in 2000 and whose distribution is governed by various conditions adopted under a REMS. In reaching that decision, the District Court made a number of findings that may negatively impact the development, approval and distribution of drug products in the United States. Further, the District Court read the standing requirements governing litigation in federal court as permitting a plaintiff to bring a lawsuit against the FDA in connection with its decision to approve an NDA or establish requirements under a REMS based on a showing that the plaintiff or its members would be harmed to the extent that FDA's drug approval decision effectively compelled the plaintiffs to provide care for patients suffering adverse events caused by a given drug.

On April 12, 2023, the District Court decision was stayed, in part, by the U.S. Court of Appeals for the Fifth Circuit. The Court of Appeals for the Fifth Circuit held oral argument in the case on May 17, 2023 and, on August 16, 2023, issued its decision. The Court of Appeals for the Fifth Circuit held that plaintiffs were likely to prevail in their claim that changes allowing for expanded access of mifepristone that FDA authorized in 2016 and 2021 were arbitrary and capricious. On September 8, 2023, the U.S. Department of Justice and a manufacturer of mifepristone filed petitions for a writ of certiorari, requesting that asked the Supreme Court to review the decision of the Court of Appeals for the Fifth Circuit. On December 13, 2023, the Supreme Court granted these petitions for writ of certiorari for the decision.

Accordingly, in connection with our currently approved products and assuming we, or any current or future collaborators, receive marketing approval for one or more of our product candidates, we, and any current or future collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we, and any current or future collaborators, are not able to comply with post-approval regulatory requirements, we, and any current or future collaborators, could have the marketing approvals for our products withdrawn by regulatory authorities and our, or any current or future collaborators', ability to market any products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

We may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products.

Any product candidate for which we obtain marketing approval will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control and manufacturing, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. In addition, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine, including the requirement to implement a risk evaluation and mitigation strategy. Accordingly, if we receive marketing approval for one or more of our product candidates, we will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we fail to comply with these requirements, we could have the marketing approvals for our products withdrawn by regulatory authorities and our ability to market any products could be limited, which could adversely affect our ability to achieve or sustain profitability.

We must also comply with requirements concerning advertising and promotion for any of our product candidates for which we obtain marketing approval. Promotional communications with respect to prescription products are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we will not be able to promote any products we develop for indications or uses for which they are not approved. The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug or biologic. Violations of the Federal Food, Drug, and Cosmetic Act, or the FDCA Act, and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may lead to investigations and enforcement actions alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws. Failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use of a product;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;

- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure or detention;
- injunctions or the imposition of civil or criminal penalties;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation; or
- litigation involving patients using our products.

Similar restrictions apply to the approval of our products in the European Union. The holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products.

Our relationships with healthcare providers, physicians and third-party payors will be subject, directly or indirectly, to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which, in the event of a violation, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription and use of our products and any product candidates for which we obtain marketing approval. Our future arrangements with healthcare providers, physicians and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered products to report payments and other transfers of value to physicians, other healthcare providers and teaching hospitals; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and transparency statutes, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require product manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

If our operations or the operations of our present and future collaborators are found to be in violation of any of the laws described above or any governmental regulations that apply to us or them, we or they may be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our or their financial results. We are developing and implementing a corporate compliance program designed to ensure that we will market and sell any future products that we successfully develop from our product candidates in compliance with all applicable laws and regulations, but we cannot guarantee that this program will protect us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Efforts to ensure that our business with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. For example, we are engaged in an ongoing effort to improve our healthcare compliance program and establish a more robust compliance infrastructure. We may fail to establish appropriate compliance measures, and even with a stronger program in place, it is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in other jurisdictions. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of European Union Member States and the UK Bribery Act 2010. Payments made to physicians in certain European Union Member States must be publicly disclosed and often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Current and future legislation or executive actions may increase the difficulty and cost for us and any current or future collaborators to obtain marketing approval of and commercialize our products or product candidates and affect the prices we, or they, may obtain.

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our drug candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any drugs for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for any approved drugs. If reimbursement of our products is unavailable or limited in scope, our business could be materially harmed.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, the ACA. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031 under the CARES Act. Pursuant to subsequent legislation, however, these Medicare sequester reductions were suspended and reduced through the end of June 2022, with the full 2% cut scheduled to resume thereafter. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our products or product candidates for which we may obtain regulatory approval or the frequency with which any such product is prescribed or used. Under current legislation, the actual reductions in Medicare payments may vary up to 4%.

Since enactment of the ACA, there have been and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the 2017 Tax Act, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, on June 17, 2021,the U.S. Supreme Court dismissed an action to challenge the constitutionality of the ACA after finding that the plaintiffs did not have standing to bring the legal action. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden revoked those Executive Orders and issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care and consider actions that will protect and strengthen that access. Under this Executive Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

We expect that these healthcare reforms, as well as other 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 any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates.

The prices of prescription pharmaceuticals in the United States and foreign jurisdictions are subject to considerable legislative and executive actions and could impact the prices we obtain for our products, if and when licensed.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of pharmaceuticals under Medicare and Medicaid, and reform government program reimbursement methodologies for products. In 2020, President Trump issued several Executive Orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most-favored-nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, CMS issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, the Department of Health and Human Services, or HHS, and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. Nine states (Colorado, Florida, Maine, New Hampshire, New Mexico, North Dakota, Texas, Vermont and Wisconsin) have passed laws allowing for the importation of drugs from Canada. Certain of these states have submitted Section 804 Importation Program proposals and are awaiting FDA approval. On January 5, 2023, the FDA approved Florida's plan for Canadian drug importation.

Further, on November 20, 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 manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors were delayed and recent legislation imposed a moratorium on implementation of the rule until January 1, 2026.

On July 9, 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. The Executive Order directed the HHS to create a plan to combat "excessive pricing of prescription pharmaceuticals and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such pharmaceuticals, and to address the recurrent problem of price gouging." On September 9, 2021, HHS released its plan to reduce pharmaceutical prices. The key features of that plan are to: (a) make pharmaceutical prices more affordable and equitable for all consumers and throughout the health care system by supporting pharmaceutical price negotiations with manufacturers; (b) improve and promote competition throughout the prescription pharmaceutical industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

More recently, on August 16, 2022, the Inflation Reduction Act, or IRA, was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Nonetheless, since CMS may establish a maximum price for these products in price negotiations, we would be fully at risk of government action if our products were to become the subject of Medicare price negotiations. Moreover, given the risk that could be the case, these provisions of the IRA may also further heighten the risk that we would not be able to achieve the expected return on our drug products or full value of our patents protecting our products if prices are set after such products have been on the market for nine years.

Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year. In addition, the IRA potentially raises legal risks with respect to individuals participating in a Medicare Part D prescription drug plan who may experience a gap in coverage if they required coverage above their initial annual coverage limit before they reached the higher threshold, or "catastrophic period" of the plan. Individuals requiring services exceeding the initial annual coverage limit and below the catastrophic period, must pay 100% of the cost of their prescriptions until they reach the catastrophic period. Among other things, the IRA contains many provisions aimed at reducing this financial burden on individuals by reducing the co-insurance and co-payment costs, expanding eligibility for lower income subsidy plans, and price caps on annual out-of-pocket expenses, each of which could have potential pricing and reporting implications.

On June 6, 2023, Merck & Co. filed a lawsuit against the HHS and CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties, including the U.S. Chamber of Commerce, Bristol Myers Squibb Company, the PhRMA, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca and Boehringer Ingelheim, also filed lawsuits in various courts with similar constitutional claims against the HHS and CMS. We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results.

Accordingly, while it is currently unclear how the IRA will be effectuated, we cannot predict with certainty what impact any federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare organizations and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

In countries outside of the United States, reimbursement and healthcare payment systems vary significantly by country and many countries have instituted price ceilings on specific products and therapies. In many countries, including those of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control and access. 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 or our collaborators may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount or if pricing is set at unsatisfactory levels, our business could be materially harmed.

Reporting and payment obligations under the Medicaid Drug Rebate Program and other governmental drug pricing programs are complex and may involve subjective decisions. Any failure to comply with those obligations could subject us to penalties and sanctions.

As a condition of reimbursement by various federal and state health insurance programs, pharmaceutical companies are required to calculate and report certain pricing information to federal and state agencies. The regulations governing the calculations, price reporting and payment obligations are complex and subject to interpretation by various government and regulatory authorities, as well as the courts. Reasonable assumptions have been made where there is lack of regulations or clear guidance and such assumptions involve subjective decisions and estimates. Pharmaceutical companies are required to report any revisions to calculations, price reporting and payment obligations previously reported or paid. Such revisions could affect liability to federal and state payers and also adversely impact reported financial results of operations in the period of such restatement.

Uncertainty exists as new laws, regulations, judicial decisions, or new interpretations of existing laws, or regulations related to our calculations, price reporting or payments obligations increases the chances of a legal challenge, restatement or investigation. If a company becomes subject to investigations, restatements, or other inquiries concerning compliance with price reporting laws and regulations, it could be required to pay or be subject to additional reimbursements, penalties, sanctions or fines, which could have a material adverse effect on the business, financial condition and results of operations. In addition, it is possible that future healthcare reform measures could be adopted, which could result in increased pressure on pricing and reimbursement of products and thus have an adverse impact on financial position or business operations.

Further, state Medicaid programs may be slow to invoice pharmaceutical companies for calculated rebates resulting in a lag between the time a sale is recorded and the time the rebate is paid. This results in a company having to carry a liability on its consolidated balance sheets for the estimate of rebate claims expected for Medicaid patients. If actual claims are higher than current estimates, the company's financial position and results of operations could be adversely affected.

In addition to retroactive rebates and the potential for 340B Program refunds, if a pharmaceutical firm is found to have knowingly submitted any false price information related to the Medicaid Drug Rebate Program to CMS, it may be liable for civil monetary penalties. Such failure could also be grounds for CMS to terminate the Medicaid drug rebate agreement, pursuant to which companies participate in the Medicaid program. In the event that CMS terminates a rebate agreement, federal payments may not be available under government programs, including Medicaid or Medicare Part B, for covered outpatient drugs.

Additionally, if a pharmaceutical company overcharges the government in connection with the Federal Supply Schedules program or Tricare Retail Pharmacy Program, whether due to a misstated Federal Ceiling Price or otherwise, it is required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against a company under the False Claims Act and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Our collaborators are also subject to similar requirements outside of the United States and thus the attendant risks and uncertainties. If our collaborators suffer material and adverse effects from such risks and uncertainties, our rights and benefits for our licensed products could be negatively impacted, which could have a material and adverse impact on our revenues.

Failure to obtain marketing approval in foreign jurisdictions would prevent our products or product candidates from being marketed abroad.

In order to market and sell our products and product candidates in the European Union and many other jurisdictions, including certain jurisdictions covered by our AffaMed collaboration, we or our third-party collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be sold in that country. We or our collaborators may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in other countries. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

Further, we could face heightened risks with respect to obtaining marketing authorization in the United Kingdom as a result of the withdrawal of the United Kingdom from the European Union, commonly referred to as Brexit. The United Kingdom is no longer part of the European Single Market and European Union Customs Union. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas under the terms of the Northern Ireland Protocol, Northern Ireland is currently subject to European Union rules. The United Kingdom and European Union have however agreed to the Windsor Framework which fundamentally changes the existing system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the United Kingdom. Once implemented, the changes introduced by the Windsor Framework will see the MHRA be responsible for approving all medicinal products destined for the United Kingdom market (i.e., Great Britain and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland.

In addition, foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, the European Union pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products (potentially reducing the duration of regulatory data protection, revising the eligibility for expedited pathways, etc.) was published on April 26, 2023. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may however have a significant impact on the pharmaceutical industry and our business in the long term.

We expect that we will also be subject to additional risks in commercializing any of our product candidates that receive marketing approval outside the United States, including tariffs, trade barriers and regulatory requirements; economic weakness, including inflation, or political instability in particular foreign economies and markets; compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; and workforce uncertainty in countries where labor unrest is more common than in the United States.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the EU General Data Protection Regulation, or the GDPR, which took effect across all member states of the European Economic Area, or EEA, in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial subjects and investigators. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States and, as a result, increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues or 20 million Euros, whichever is greater, and it also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that European Union member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data. Similar laws and regulations have been approved, or are expected to be approved, in several jurisdictions beyond the European Union including the UK Data Protection Act 2018.

Similar actions are either in place or under way in the United States. There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act, or CCPA—which went into effect on January 1, 2020—is creating similar risks and obligations as those created by GDPR, though the CCPA does currently exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects, known as the Common Rule. The CCPA also has been amended through a recent referendum in California that creates additional obligations beginning in 2023. At least two other states have adopted, and many other states are considering, similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with federal and state laws (both those currently in effect and future legislation) regarding privacy and security of personal information could expose us to fines and penalties under such laws. There also is the threat of consumer class actions related to these laws and the overall protection of personal data. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with these requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in applicable jurisdictions. These changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

Our internal information technology systems, or those of our vendors, collaborators, contractors, consultants, or other third parties may fail or suffer security breaches, which could result in a material disruption of our product development programs, compromise sensitive information related to our business or prevent us from accessing critical information, trigger contractual and legal obligations, potentially exposing us to liability, reputational harm or otherwise adversely affecting our business and financial results.

We are dependent upon information technology systems, infrastructure and data to operate our business. In the ordinary course of business, we collect, store and transmit large amounts of confidential information, including personal information and information relating to intellectual property, on internal and external information systems and through the information systems of our vendors, collaborators, contractors, consultants, or other third parties. It is critical that we, our vendors, collaborators, contractors, consultants, or other third parties, do so in a secure manner to maintain the availability, security, confidentiality, privacy and integrity of such confidential information.

Despite the implementation of security measures, our internal information technology systems and those of third parties are vulnerable to damage from computer viruses, malware, computer hackers, malicious code, employee error, theft or misuse, denial-of-service attacks, sophisticated nation-state supported actors, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such systems are also vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, our collaborators, contractors, consultants, vendors, and other third parties, or from cyberattacks by malicious third parties over the Internet or through other mechanisms. Cyberattacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyberattacks could include the deployment of harmful malware, ransomware, denial of service attacks, unauthorized access to or deletion of files, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Cyberattacks also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient. We may not be able to anticipate all types of security threats, and we may not be able to implement preventive measures effective against all such security threats. The techniques used by cyber criminals change frequently, may not be recognized until launched, and can originate from a wide variety of sources, including outside groups such as external service providers, organized crime affiliates, terrorist organizations or hostile foreign governments or agencies. We cannot guarantee that the measures we have taken to date, and actions we may take in the future, will be sufficient to prevent any future breaches.

While we have not experienced any such material system failure, accident, cyberattack or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs, clinical trials and business operations, whether due to a loss of our trade secrets or other proprietary or confidential information or other similar disruptions, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of clinical trial data from clinical trials could result in delays or termination of our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, as risks with respect to our information systems continue to evolve, we will incur additional costs to maintain the security of our information systems and comply with evolving laws and regulations pertaining to cybersecurity and related areas.

To the extent that any disruption or security breach were to result in a loss of, or damage to, our or our vendors', collaborators' or other contractors' or consultants' data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, including litigation exposure, penalties and fines, we could become the subject of regulatory action or investigation, enrollment in our clinical trials could be negatively affected, our competitive position and reputation could be harmed and the further development and commercialization of our product candidates could be delayed. As a result of such an event, we may be in breach of our contractual obligations. Furthermore, any such event that leads to unauthorized access, use, or disclosure of personal information, including personal information regarding our customers or employees, could harm our reputation, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information, which could result in significant legal and financial exposure and reputational damages. Any of the above could have a material adverse effect on our business, financial condition, results of operations or prospects.

The financial exposure from the events referenced above could either not be insured against or not be fully covered through any insurance that we maintain and could have a material adverse effect on our business, financial condition, results of operations or prospects. In addition, we cannot be sure that our existing insurance coverage will continue to be available on acceptable terms or that our insurers will not deny coverage as to any future claim. There can be no assurance that the limitations of liability in our contracts would be enforceable or adequate or would otherwise protect us from liabilities or damages as a result of the events referenced above.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain products outside of the United States and require us to develop and implement costly compliance programs.

If we expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The Securities and Exchange

Commission also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We remain highly dependent on the research and development, clinical and business development expertise of our principal members of our management, scientific and clinical team, including Pravin Dugel, M.D., our Executive Chairman, and Antony Mattessich, our President and Chief Executive Officer. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel is critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by other entities and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

Risks Related to Our Common Stock

Provisions in our corporate charter documents and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our certificate of incorporation and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- provide for a classified board of directors such that only one of three classes of directors is elected each year;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- provide for advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;

- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and

- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our certificate of incorporation or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

We have been subject to legal proceedings related to the decline in our stock price, and we could be subject to similar legal proceedings in the future, which could distract our management and could result in substantial costs or large judgments against us.

In the past, securities class action litigation has often been brought against companies following periods of volatility in the market prices of their securities.

In July 2017, we experienced a decline in our stock price following our announcement that we had received notice of the FDA's determination that it could not approve our NDA for DEXTENZA in its then present form. In 2017 and 2018, class action lawsuits were filed against us and certain of our executive officers and shareholder derivative actions were filed against certain of our executive officers and directors, and two of our investors and against the company as a nominal defendant. While these legal proceedings were ultimately resolved in our and/or the applicable defendants' favor, they were distracting and were both time-consuming and costly to defend. We may be the target of similar proceedings in the future. We also may face securities class-action litigation if we cannot obtain regulatory approvals for or if we otherwise fail to commercialize our products or product candidates successfully.

In connection with any such legal proceedings, we could incur substantial costs and such costs and any related settlements or judgments may not be covered by insurance. We could also suffer an adverse impact on our reputation and a diversion of management's attention and resources, which could cause serious harm to our business, operating results and financial condition.

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for holders of our common stock.

Our stock price has been, and in the future may be, volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance. As a result of this volatility, our stockholders may not be able to sell their common stock at or above the price at which they purchased it. The market price for our common stock may be influenced by many factors, including:

- our success in commercializing DEXTENZA and any product candidates for which we obtain marketing approval;

- the success of competitive products or technologies;

- results of clinical trials of our product candidates and the product candidates of our competitors;

- regulatory or legal developments in the United States and other countries;

- developments or disputes concerning patent applications, issued patents or other proprietary rights;

- the recruitment or departure of key scientific or management personnel;

- the results of our efforts and the efforts of our current and future collaborators to discover, develop, acquire or in-license and out-license additional products, product candidates or technologies for the treatment of ophthalmic diseases or conditions, the costs of commercializing any such products and the costs of development of any such product candidates or technologies and any potential dilution to our shareholders as a result of these efforts;

- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;

- variations in our financial results or those of companies that are perceived to be similar to us;

- the ability to secure third-party reimbursement for our products or product candidates;

- market conditions in the pharmaceutical and biotechnology sectors; and

- the other factors described in this "Risk Factors" section.

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

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of our Credit Agreement and any future debt agreements that we may enter into, may preclude us from paying dividends without the lenders' consent or at all. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.

Item 1B. Unresolved Staff Comments

Not Applicable.

Item 1C. Cybersecurity

We have certain processes for assessing, identifying and managing cybersecurity risks, which are built into our overall risk management program and are designed to help protect our information assets and operations from internal and external cyber threats and to protect the information of employees, customers, vendors, and other individuals, such as subjects enrolled in our clinical trials, from unauthorized access or attack, as well as secure our networks and systems. We have designed our processes based on, and periodically assess our processes against, the National Institute of Standards and Technology Cybersecurity Framework Special Publication 800-53, 800-61, rev 2, or the NIST Framework. This does not imply that we meet any particular technical standards, specifications, or requirements of the NIST Framework, only that we use these standards as a guide to help us identify, assess, and manage cybersecurity risks relevant to our business. Our processes for assessing, identifying and managing cybersecurity risks include physical, procedural and technical safeguards, a cybersecurity incident response plan, regular tests on our systems, incident simulations and routine review of our policies and procedures to identify risks and improve our practices. We engage certain external parties, including computer security firms, to assist us with the identification, verification, and validation of cybersecurity risks, and to support mitigation efforts if necessary. We consider the internal risk oversight programs of third-party service providers before engaging them in order to help protect us from any related vulnerabilities.

We do not believe that there are currently any known risks from cybersecurity threats that are reasonably likely to materially affect us or our business strategy, results of operations or financial condition.

The Audit Committee of our board of directors provides direct oversight over cybersecurity risk and provides updates to the board of directors regarding such oversight as deemed necessary. The Audit Committee receives periodic updates from management regarding cybersecurity matters and is notified between such updates regarding significant new cybersecurity threats or incidents.

Our management team is responsible for day-to-day assessment and management of cybersecurity risks. On our management team, our Chief Financial Officer, or CFO, leads the operational oversight of company-wide cybersecurity strategy, policy, standards and processes and works across relevant departments to assess and help prepare us and our employees, customers, vendors and other individuals to address cybersecurity risks. Our CFO has approximately 10 years of experience managing information technology teams of operating companies in the biotechnology industry. Our CFO leads a cross-functional Cybersecurity Committee, consisting of executive-level leaders and other management-level individuals with the requisite skills and education, that assists the CFO with carrying out these duties. Collectively, the members of our Cybersecurity Committee have notable experience in managing information security, possess the education and skills to fulfill these duties, and attend periodic trainings as necessary.

In an effort to deter and detect cyber threats, we provide all employees, including part-time and temporary employees, with periodic training, including training related to data protection, cybersecurity and incident response, and prevention and compliance, which covers timely and relevant topics, including social engineering, phishing, password protection, confidential data protection, asset use and mobile security, and educates employees on the importance of reporting all incidents immediately. We also use technology-based tools to mitigate cybersecurity risks and to bolster our employee-based cybersecurity programs.

Item 2. Properties

Our facilities consist of leased office space, laboratory space and manufacturing facilities in Bedford, Massachusetts. We occupy approximately 121,000 square feet of space. The lease for approximately 71,000 square feet of this space expires in July 2027, the lease for approximately 30,000 square feet of this space expires in March 2024, and the lease for approximately 20,000 square feet of this space, which includes our manufacturing facility, expires in July 2028. We do not intend to renew the lease that expires in March 2024 nor do we intend to lease new space, as we believe that our remaining current facilities are suitable and adequate to meet our current needs.

Item 3. Legal Proceedings

From time to time, we may become involved in various lawsuits and legal proceedings which arise in the ordinary course of business. However, litigation is subject to inherent uncertainties, and an adverse result in these or other matters may arise from time to time that may harm our business. We are not presently a party to any material legal proceedings, nor to the knowledge of management are any material legal proceedings threatened against us.

Item 4. Mine Safety Disclosures

Not Applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer's Purchases of Equity Securities

Our common stock has been publicly traded on the Nasdaq Global Market under the symbol "OCUL" since July 25, 2014.

Holders

As of March 7, 2024, there were approximately 29 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

Dividends

We have never declared or paid cash dividends on our common stock, and we do not expect to pay any cash dividends on our common stock in the foreseeable future. In addition, the terms of our existing credit facility preclude us from paying cash dividends without the consent of our lenders.

Securities Authorized for Issuance under Equity Compensation Plans

The information required by this item will be set forth in the definitive proxy statement we will file in connection with our 2024 Annual Meeting of Stockholders and is incorporated by reference herein.

Recent Sales of Unregistered Securities

We did not sell any shares of our common stock, shares of our preferred stock or warrants to purchase shares of our stock, or grant any stock options or restricted stock awards, during the year ended December 31, 2023 that were not registered under the Securities Act of 1933, as amended, or the Securities Act, and that have not otherwise been described in an Annual Report on Form 10-K or a Quarterly Report on Form 10-Q.

Purchase of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

Item 6. [Reserved.]

Item 7. 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 consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties and should be read together with the "Risk Factors" section of this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

Our Company

We are a biopharmaceutical company committed to enhancing people's vision and quality of life through the development and commercialization of innovative therapies for diseases and conditions of the eye, with a specific focus on retinal disease. Our program for retinal disease is led by AXPAXLI (axitinib intravitreal implant, also known as OTX-TKI), which is based on our ELUTYX proprietary bioresorbable hydrogel-based formulation technology. We are currently conducting a pivotal Phase 3 clinical trial to evaluate AXPAXLI for the treatment of wet age-related macular degeneration, or wet AMD, which we refer to as the SOL-1 trial, and a Phase 1 clinical trial for the treatment of diabetic retinopathy. Our clinical portfolio also includes PAXTRAVA (travoprost intracameral implant, also known as OTX-TIC), which is currently in Phase 2 clinical development for the treatment of primary open-angle glaucoma, or OAG, or ocular hypertension, or OHT.

Our expertise in the formulation, development and commercialization of innovative therapies and our ELUTYX platform supported the development and launch of our first commercial drug product, DEXTENZA, a corticosteroid approved by the U.S. Food and Drug Administration, or FDA, for the treatment of ocular inflammation and pain following ophthalmic surgery and ocular itching associated with allergic conjunctivitis. We are also developing two other clinical-stage assets, OTX-DED (dexamethasone intracanalicular insert) for the short-term treatment of the signs and symptoms of dry eye disease, and OTX-CSI (cyclosporine intracanalicular insert) for the chronic treatment of dry eye disease, which we collectively refer to as our Dry Eye Programs, and several preclinical programs.

Key Business and Financial Developments

Board of Directors and Leadership Updates

In February 2024, we expanded our leadership team and added Pravin Dugal, M.D. as Executive Chairman on a full-time basis. We also added Jeffrey Heier, M.D. as Chief Scientific Officer, Peter Kaiser, M.D. as Medical Director, both on a part-time basis, and Sanjay Nayak, MBBS, PhD as Chief Strategy Officer on a full-time basis. We believe the contribution of these acknowledged strategic and clinical experts will put the Company on track to be a leader in retina care for wet AMD, non-proliferative diabetic retinopathy, or NPDR, and other conditions.

In connection with these additions, Charles Warden transitioned from Chairman of the Board to Lead Independent Director. To enable full transitions to their new operating roles, Dr. Heier resigned from his positions with us as a Board Director and Advisor – Retina, and Dr. Kaiser resigned from his position as Chief Medical Advisor – Retina. In addition, Peter Jarrett, PhD has begun the new role of Chief Technical Officer. Rabia Gurses Ozden, M.D. will continue in her role as Chief Medical Officer.

AXPAXLI

We are conducting a pivotal Phase 3 clinical trial as the first of two planned pivotal trials for the treatment of wet AMD, which we refer to as the SOL-1 trial. The first subjects in the SOL-1 trial were screened and received their first aflibercept injection in February 2024. We expect to complete enrollment of the SOL-1 trial by the end of the first quarter of 2025. Subject to agreement with the FDA, we intend to commence screening of a second pivotal Phase 3 clinical trial for the treatment of wet AMD, which we refer to as the SOL-2 trial, by the first quarter of 2025.

In September 2023, we submitted a request for a Special Protocol Assessment, or SPA, to the FDA to determine whether the proposed clinical protocol and the statistical analysis plan for the SOL-1 trial adequately addressed scientific and regulatory requirements for a clinical trial that could support a marketing application. We received an agreement letter regarding the overall trial design from the FDA under the SPA in October 2023. In December 2023, we submitted an amendment to the SPA to the FDA to broaden the inclusion criteria for subjects in the SOL-1 trial and to reflect our intention to evaluate a single optimized implant of AXPAXLI with a drug load of 450 µg of a more soluble form of axitinib in the SOL-1 trial, or the SPA Agreement Modification. We received an agreement letter regarding the SPA Agreement Modification in January 2024. If we were to obtain favorable results from both the SOL-1 trial and the SOL-2 trial, we plan to submit a New Drug Application, or NDA, with the FDA for marketing approval.

In June 2023, we presented 12-month data from the clinical trial of AXPAXLI for the treatment of wet AMD in the United States at the Clinical Trials at the Summit 2023 conference sponsored by the American Society of Retina Specialists.

We initiated a U.S.-based multicenter, double-masked, randomized, parallel group study evaluating the safety, tolerability and biological activity of AXPAXLI in patients with moderately severe to severe NPDR without DME, which we refer to as the HELIOS trial, in the fourth quarter of 2022. We dosed our first subject in February 2023. We announced the completion of enrollment in the HELIOS trial in June 2023 and expect to provide 9-month topline data in the second quarter of 2024. Subject to favorable topline data from the HELIOS trial and agreement with the FDA, we intend to commence a pivotal Phase 3 clinical trial.

PAXTRAVA

We are conducting a Phase 2 clinical trial evaluating the safety, tolerability and efficacy of PAXTRAVA for the treatment of subjects with primary OAG or OHT. We completed enrollment of this Phase 2 clinical trial in July 2023. We have started a pilot repeat-dose substudy in the Phase 2 clinical trial to evaluate the safety of a repeat, sustained release dose in a small subset of subjects with OAG or OHT. We plan to provide topline data from this Phase 2 clinical trial at the American Society of Cataract and Refractive Surgery 2024 Annual Meeting in April 2024. Subject to favorable topline data, we intend to evaluate our strategic alternatives in moving the PAXTRAVA program into pivotal Phase 3 clinical trials.

Commercial

Our net product revenue was $57.9 million for the year ended December 31, 2023, reflecting an increase of $7.4 million or 14.7% over the year ended December 31, 2022.

In November 2023, the Centers for Medicare and Medicaid Services, or CMS, released the final rulemaking for CY 2024 under the Outpatient Prospective Payment System, or OPPS. The final rule confirms that DEXTENZA will continue to be separately reimbursed by Medicare in the ambulatory surgical center, or ASC, setting under the non-opioid pain provision; and that CPT 68841, the code that describes the insertion of DEXTENZA, maintains a Q1 status indicator.

We believe that DEXTENZA is currently used in less than 5% of cataract procedures and that commercial growth may be driven by a continued focus on sales to ASCs, specifically strategic accounts that own and control multiple ASCs.

2024 Private Placement

In February 2024, concurrent with the *Board of Directors and Leadership Updates* detailed above, we sold 32,413,560 shares of our common stock at $7.52 per share and, in lieu of common stock to certain investors, pre-funded warrants to purchase up to an aggregate of 10,805,957 shares of our common stock at a price of $7.519 per pre-funded warrant for aggregate gross proceeds of approximately $325.0 million, before deducting placement agent fees and other offering expenses, or the 2024 Private Placement. Each pre-funded warrant has an exercise price of $0.001 per share, is currently exercisable and will remain exercisable until exercised in full.

2023 Equity Financing

In December 2023, we completed an underwritten public offering of 35,420,000 shares of our common stock at a public offering price of $3.25 per share. The total gross proceeds of the public offering were approximately $115.1 million, before deducting underwriting discounts and commissions and other offering expenses payable by us, resulting in net proceeds of approximately $107.7 million.

In 2023, we sold 1,514,926 shares of our common stock under our Open Market Sale Agreement with Jefferies LLC, or Jefferies, resulting in gross proceeds to us of $9.9 million, and net proceeds, after accounting for issuance costs, of $9.5 million.

2023 Debt Financing

In August 2023, we entered into a credit and security agreement, or the Barings Credit Agreement, with Barings Finance LLC, or Barings, as administrative agent, and the lenders party thereto, providing for a secured term loan facility for us, or the Barings Credit Facility, in the aggregate principal amount of $82.5 million. We borrowed the full amount of $82.5 million at closing and received proceeds of $77.3 million, after the application of an original issue discount and fees.

In March 2019, we issued $37.5 million of unsecured senior subordinated convertible notes, or the Convertible Notes. Concurrently with entering into the Barings Credit Agreement, in August 2023, we and the holders of the Convertible Notes extended the maturity of the Convertible Notes, which would otherwise have matured on March 1, 2026, to a date 91 days following the maturity of the indebtedness under the Barings Credit Facility.

In connection with entering the Barings Credit Facility, in August 2023, we paid MidCap Financial Trust, as administrative agent, and our other lenders an aggregate of $26.2 million in satisfaction of our obligations under our prior credit facility, which we refer to as the MidCap Credit Facility.

Collaborations

In the second quarter of 2023, we received a $1 million milestone payment from our collaboration partner AffaMed Therapeutics Limited, or AffaMed, upon the approval of AffaMed's clinical trial application to initiate a Phase 3 registrational study in China to investigate the efficacy and safety of DEXTENZA in subjects following ophthalmic surgery by China's National Medical Products Administration. In the second quarter of 2022, we received a $2 million clinical support payment in connection with dosing the first subject in a Phase 2 clinical trial evaluating PAXTRAVA for the treatment of OAG or OHT.

Components of our Financial Performance

Revenue

We recognize product revenue when we sell DEXTENZA in the United States to a network of specialty distributors on a direct basis, who then resell the product to ASCs and hospital out-patient departments, or HOPDs, and physicians' offices, and when we sell DEXTENZA on a direct basis to a small number of ASCs. We refer to these resales from the specialty distributors to the ASCs and HOPDs as in-market unit sales. We record DEXTENZA product sales net of estimated chargebacks, rebates, distribution fees and product returns. These deductions are generally referred to as gross-to-net deductions.

Operating Expenses

Cost of Product Revenue

Cost of product revenue consists primarily of costs of DEXTENZA product revenue, which include:

- Direct materials costs;
- Royalties;

- Direct labor, which includes employee-related expenses, including salaries, related benefits and payroll taxes, and stock-based compensation expense for employees engaged in the production process;

- Manufacturing overhead costs, which includes rent, depreciation, and indirect labor costs associated with the production process;

- Transportation costs; and

- Cost of scrap material.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for the development of our product candidates, which include:

- employee-related expenses, including salaries, related benefits and payroll taxes, travel and stock-based compensation expense for employees engaged in research and development, clinical and regulatory and other related functions;

- expenses incurred in connection with the clinical trials of our product candidates, including with the investigative sites that conduct our clinical trials and under agreements with contract research organizations, or CROs;

- expenses relating to regulatory activities, including filing fees paid to the FDA for our submissions for product approvals;

- expenses associated with developing our pre-commercial manufacturing capabilities and manufacturing clinical study materials;

- ongoing research and development activities relating to our core bioresorbable hydrogel technology and improvements to this technology;

- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and supplies;

- costs relating to the supply and manufacturing of product inventory, prior to approval by the FDA or other regulatory agencies of our products; and

- expenses associated with preclinical development activities.

We expense research and development costs as incurred. We recognize external development costs based on an evaluation of the progress to completion of specific tasks using information provided to us by our vendors and our clinical investigative sites.

Our direct research and development expenses are tracked on a program-by-program basis and consist primarily of external costs, such as fees paid to investigators, consultants, central laboratories and CROs in connection with our clinical trials and regulatory fees. We do not allocate employee and contractor-related costs, costs associated with our proprietary bioresorbable hydrogel-based formulation technology ELUTYX, costs related to manufacturing or purchasing clinical trial materials, and facility expenses, including depreciation or other indirect costs, to specific product development programs because these costs are deployed across multiple product development programs and, as such, are not separately classified. We use internal resources in combination with third-party CROs, including clinical monitors and clinical research associates, to manage our clinical trials, monitor subject enrollment and perform data analysis for many of our clinical trials. These employees work across multiple development programs and, therefore, we do not track their costs by program.

The successful development and commercialization of our products or product candidates is highly uncertain. This is due to the numerous risks and uncertainties associated with product development and commercialization, including the uncertainty of:

- the scope, progress, outcome and costs of our clinical trials and other research and development activities;
- the timing, receipt and terms of any marketing approvals;
- the efficacy and potential advantages of our products or product candidates compared to alternative treatments, including any standard of care;
- the market acceptance of our products or product candidates; and
- significant and changing government regulation.

Any changes in the outcome of any of these variables with respect to the development of our product candidates in clinical and preclinical development could mean a significant change in the costs and timing associated with the development of these product candidates. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials or other testing beyond those that we currently expect or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development of that product candidate. We anticipate that our research and development expenses will increase in the future as we support our continued development of our product candidates.

Selling and Marketing Expenses

Selling and marketing expenses consist primarily of salaries and related costs for personnel in selling and marketing functions as well as consulting, advertising and promotion costs.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs, including stock-based compensation, for personnel in executive, finance, information technology, human resources and administrative functions. General and administrative expenses also include insurance, facility-related costs and professional fees for legal, patent, consulting and accounting and audit services.

Other Income (Expense)

Interest Expense. Interest expense is incurred on our debt. For the year ended December 31, 2023, our interest-bearing debt included the Barings Credit Facility ($82.5 million outstanding principal since August 2, 2023), the Convertible Notes ($37.5 million outstanding principal) and the notes payable under the MidCap Credit Facility ($25.0 million outstanding principal through August 2, 2023, no outstanding principal thereafter).

Change in Fair Value of Derivative Liabilities. In August 2023, in connection with entering into the Barings Credit Agreement, we identified an embedded derivative liability, which we are required to measure at fair value at inception and then at the end of each reporting period until the embedded derivative is settled. In 2019, in connection with the issuance of our Convertible Notes, we identified an embedded derivative liability, which we are required to measure at fair value at inception and then at the end of each reporting period until the embedded derivative is settled. The changes in fair value of these derivative liabilities are recorded through the consolidated statement of operations and comprehensive loss and are presented under the caption change in fair value of derivative liabilities.

Gains and Losses from Debt Extinguishment. In August 2023, we amended the Convertible Notes and accounted for the amendment as an extinguishment of debt in accordance with the guidance in Accounting Standards Codification Topic 470-50 *Debt*. Application of this accounting standard resulted in a gain on extinguishment. In August 2023, we also extinguished our obligations under the MidCap Credit Facility, resulting in a loss on extinguishment.

Results of Operations

Comparison of the Years Ended December 31, 2023 and December 31, 2022

The following table summarizes our results of operations for the years ended December 31, 2023 and 2022:

	Year Ended December 31, 2023	Year Ended December 31, 2022	Increase (Decrease)
		(in thousands)	
Revenue:			
Product revenue, net	$ 57,870	$ 50,457	$ 7,413
Collaboration revenue	573	1,037	(464)
Total revenue, net	58,443	51,494	6,949
Costs and operating expenses:			
Cost of product revenue	5,281	4,540	741
Research and development	61,055	53,462	7,593
Selling and marketing	40,549	39,922	627
General and administrative	33,940	32,224	1,716
Total costs and operating expenses	140,825	130,148	10,677
Loss from operations	(82,382)	(78,654)	(3,728)
Other income (expense):			
Interest income	3,983	798	3,185
Interest expense	(11,338)	(7,022)	(4,316)
Change in fair value of derivative liabilities	(5,188)	13,841	(19,029)
Gains and losses on extinguishment of debt, net	14,190	—	14,190
Other expense, net	(1)	(1)	—
Total other income, net	1,646	7,616	(5,970)
Net loss	$ (80,736)	$ (71,038)	$ (9,698)

Product Revenue, net

Our product revenue, net was $57.9 million and $50.5 million for the years ended December 31, 2023 and 2022, respectively, reflecting an increase of $7.4 million year-over-year. All of our product revenue, net, was attributable to sales of DEXTENZA.

Our total gross-to-net provisions for the years ended December 31, 2023 and 2022 were 30.1% and 24.9%, respectively, of gross DEXTENZA product sales.

Collaboration Revenue

We recognized $0.6 million of collaboration revenue related to the performance obligation under our license agreement with AffaMed to conduct a Phase 2 clinical trial of PAXTRAVA during the year ended December 31, 2023 compared to $1.0 million in the year ended December 31, 2022. We recognize collaboration revenue based on a cost-to-cost method.

Research and Development Expenses

	Year Ended December 31, 2023	2022	Increase (Decrease)
		(in thousands)	
Direct research and development expenses by program:			
AXPAXLI for wet AMD	8,750	5,296	3,454
PAXTRAVA for glaucoma or ocular hypertension	3,600	2,835	765
AXPAXLI for diabetic retinopathy	$ 2,868	$ 659	$ 2,209
DEXTENZA for post-surgical ocular inflammation and pain	2,224	1,649	575
OTX-DED for the short-term treatment of the signs and symptoms of dry eye disease	837	328	509
OTX-CSI for treatment of dry eye disease	161	453	(292)
DEXTENZA for ocular itching associated with allergic conjunctivitis	—	21	(21)
Preclinical programs	1,501	1,947	(446)
Unallocated expenses:			
Personnel costs	27,068	25,106	1,962
All other costs	14,046	15,168	(1,122)
Total research and development expenses	$ 61,055	$ 53,462	$ 7,593

Research and development expenses were $61.1 million and $53.5 million for the years ended December 31, 2023 and 2022, respectively, reflecting an increase of $7.6 million year-over-year.

Within research and development expenses, expenses for clinical programs increased $7.2 million, unallocated expenses increased $0.8 million, and expenses for preclinical programs decreased $0.4 million.

For the year ended December 31, 2023, we incurred $18.4 million in direct research and development expenses for our products and product candidates compared to $11.2 million for the year ended December 31, 2022. The increase of $7.2 million is related to timing and conduct of our various clinical trials for our product candidates, including the initiation of the SOL-1 trial and the HELIOS trial, and development activities related to our preclinical programs.

We expect that clinical trial expenses for our product candidates will increase for 2024 and beyond, as we progress with the SOL-1 trial, the HELIOS trial, and the ongoing Phase 2 clinical trial of PAXTRAVA for the treatment of primary OAG or OHT, and as we initiate the planned SOL-2 trial of AXPAXLI in the first quarter of 2025, and as we, subject to favorable topline data from the HELIOS trial and agreement with the FDA, intend to commence a pivotal Phase 3 clinical trial of AXPAXLI for NPDR as a next step of clinical development.

Selling and Marketing Expenses

	Year Ended December 31, 2023	2022	Increase (Decrease)
		(in thousands)	
Personnel related (including stock-based compensation)	$ 27,434	$ 26,679	$ 755
Professional fees	8,287	9,077	(790)
Facility related and other	4,828	4,166	662
Total selling and marketing expenses	$ 40,549	$ 39,922	$ 627

Selling and marketing expenses were $40.5 million and $39.9 million for the years ended December 31, 2023 and 2022, respectively, reflecting an increase of $0.6 million year-over-year.

The increase was primarily due to an increase of $0.8 million in personnel costs, including stock-based compensation, as we expanded our field-based team to support the commercialization of DEXTENZA, and an increase in facility-related and other costs of $0.7 million, partially offset by a decrease in professional fees, including consulting, trade shows, and conferences, of $0.8 million.

We expect our selling and marketing expenses to continue to increase for the remainder of 2024 and beyond as we continue to support the commercialization of DEXTENZA.

General and Administrative Expenses

	Year Ended December 31, 2023	2022	Increase (Decrease)
		(in thousands)	
Personnel related (including stock-based compensation)	$ 21,356	$ 18,227	$ 3,129
Professional fees	10,821	11,634	(813)
Facility related and other	1,763	2,363	(600)
Total general and administrative expenses	$ 33,940	$ 32,224	$ 1,716

General and administrative expenses were $33.9 million and $32.2 million for the years ended December 31, 2023 and 2022, respectively, reflecting an increase of $1.7 million year-over-year.

The increase was primarily due to an increase of $3.1 million in personnel related costs including stock-based compensation, which was partially offset by a decrease in professional fees of $0.8 million and a decrease of $0.6 million in facility related and other costs.

We anticipate that our general and administrative expenses will increase in the future as we support our continued development and commercialization of our product candidates. We also anticipate that we will continue to incur increased accounting, audit, legal, intellectual property, regulatory, compliance, director and officer insurance costs as well as investor and public relations expenses associated with being a public company.

Other Income (Expense), Net

Interest Income. Interest income was $4.0 million and $0.8 million for the years ended December 31, 2023 and 2022, respectively, reflecting an increase of $3.2 million year-over-year. The increase is primarily due to a higher average balance of cash and cash equivalents held by us, and higher interest rates.

Interest Expense. Interest expense was $11.3 million and $7.0 million for the years ended December 31, 2023 and 2022, respectively, reflecting an increase of $4.3 million year-over-year. The increase is primarily due to higher balances of debt outstanding as a result of us drawing $82.5 million of debt under the Barings Credit Facility in August 2023, partially offset by us paying off the MidCap Credit Facility of $25.0 million in August 2023.

Change in Fair Value of Derivative Liabilities. We recognized a loss from the change in fair values of our derivative liabilities of $5.2 million for the year ended December 31, 2023, compared to a gain of $13.8 million for the year ended December 31, 2022. The net loss for 2023 comprises of a loss of $4.5 million from the change in the fair value of the derivative liability related to a conversion option embedded in the Convertible Notes and $0.9 million related to royalty fees under the Barings Credit Agreement that we paid or accrued, partially offset by a gain of $0.2 million from the change in the fair value of the derivative liability related to the Barings Credit Agreement. The net gain for 2022 results solely from the change in the fair value of the derivative liability related to the Conversion Option. We cannot predict how the fair value of the derivative liabilities will change in 2024 and beyond.

Gains and losses on extinguishment of debt, net. We recognized a gain from accounting for the modification of the Convertible Notes as an extinguishment of $14.9 million, partially offset by a loss from extinguishment of the MidCap Credit Facility of $0.7 million.

Comparison of the Years Ended December 31, 2022 and 2021

A discussion of changes in our results of operations during the year ended December 31, 2022 compared to the year ended December 31, 2021 has been omitted from this Annual Report on Form 10-K but may be found in “Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations” in our Annual Report on Form 10-K for the year ended December 31, 2022, filed with the SEC on March 6, 2023, which discussion is incorporated herein by reference and which is available free of charge on the SECs website at www.sec.gov.

Liquidity and Capital Resources

Sources of Liquidity

We have financed our operations primarily through private placements of our preferred stock, public offerings and private placements of our common stock, borrowings under credit facilities, the private placements of our convertible notes, and sales of our products.

As of December 31, 2023, we had cash and cash equivalents of $195.8 million; outstanding notes payable with a principal amount of $82.5 million par value under the Barings Credit Facility, and outstanding Convertible Notes of $37.5 million par value plus total unpaid interest obligations related to the amounts outstanding under the Barings Credit Facility and the Convertible Notes of $11.7 million.

2023 Equity Financing

On December 18, 2023, we completed an underwritten public offering of 35,420,000 shares of our common stock at a public offering price of $3.25 per share, which includes 4,620,000 shares issued upon the exercise in full by the underwriters of their option to purchase additional shares of common stock in the public offering at the public offering price, less underwriting discounts and commissions. The total gross proceeds of the public offering were approximately $115.1 million, before deducting underwriting discounts and commissions and other offering expenses payable by us, resulting in net proceeds of approximately $107.7 million.

In 2023, we sold 1,514,926 shares of our common stock under our Open Market Sale Agreement with Jefferies, resulting in gross proceeds to us of $9.9 million, and net proceeds, after accounting for issuance costs, of $9.5 million.

2023 Debt Financing

On August 2, 2023, or the Closing Date, we entered into the Barings Credit Agreement, with Barings, as administrative agent, and the lenders party thereto, providing for the Barings Credit Facility, in the aggregate principal amount of $82.5 million, or the Total Credit Facility Amount. We borrowed the full amount of $82.5 million at closing and received proceeds of $77.3 million, after the application of an original issue discount and fees. Indebtedness under the Barings Credit Facility matures on the earlier to occur of (i) the six-year anniversary of the Closing Date and (ii) the date that is 91 days prior to the maturity date for our Convertible Notes.

Indebtedness under the Barings Credit Facility incurs interest at a Secured Overnight Financing Rate, or SOFR, based rate, subject to a minimum 1.50% floor, plus 6.75%. We are obligated to make interest payments on our indebtedness under the Barings Credit Facility on a monthly basis, commencing on the Closing Date; to pay annual administration fees; and to pay, on the maturity date, any principal and accrued interest that remains outstanding as of such date. In addition, we are obligated to pay a fee, which we refer to as the Royalty Fee, in an amount equal to the Total Credit Facility Amount, which amount shall be reduced by the total amount of interest and principal prepayment fees paid under the Barings Credit Agreement. We are required to pay the Royalty Fee in installments to Barings, for the benefit of the lenders, on a quarterly basis in an amount equal to three and one-half percent (3.5%) of the net sales of DEXTENZA occurring during such quarter, subject to the terms, conditions and limitations specified in the Barings Credit Agreement, until the Royalty Fee is paid in full. The Royalty Fee is due and payable upon a change of control of the company. In the event we complete a change of control transaction or sell all or substantially all of our assets on or prior to the twelve-month anniversary of the Closing Date, the Royalty Fee is subject to a reduction to an amount that is equal to (i) 20% of the Total Credit Facility Amount, in the event that a signed letter of intent evidencing such transaction was entered into by us on or prior to the date that is six months after the Closing Date and (ii) 30% of the Total Credit Facility Amount, in the event that a signed letter of intent evidencing such transaction was entered into by us after the date that is six months, but before the date that is twelve months, after the Closing Date. We may, at our option, prepay any or all of the Royalty Fee at any time without penalty. In connection with the Barings Credit Agreement, we have granted the lenders a first-priority security interest in all of our assets, including our intellectual property, subject to certain agreed-upon exceptions. The Barings Credit Agreement includes negative covenants restricting us from making payments to the holders of the Convertible Notes except in connection with a proposed conversion to equity and with respect to certain permitted expenses and requiring us to maintain a minimum liquidity amount of $20.0 million. The Barings Credit Agreement also includes customary affirmative and negative covenants.

In March 2019, we issued the Convertible Notes pursuant to a note purchase agreement, or the Purchase Agreement, with Cap 1 LLC, an affiliate of Summer Road LLC. Concurrently with entering into the Barings Credit Agreement, on August 2, 2023, we and the holders of the Convertible Notes extended the maturity of the Convertible Notes, which would otherwise have matured on March 1, 2026, to a date 91 days following the maturity of the indebtedness under the Barings Credit Facility. The Convertible Notes, as amended, accrue interest at an annual rate of 6% of its outstanding principal amount, payable at maturity, unless earlier converted, repurchased or redeemed. The holders of the Convertible Notes may convert all or part of the outstanding principal amount of their Convertible Notes into shares of our common stock, par value $0.0001 per share, prior to maturity and provided that no conversion results in a holder beneficially owning more than 19.99% of our issued and outstanding common stock. The conversion rate is initially 153.8462 shares of our common stock per $1,000 principal amount of the Convertible Notes, which is equivalent to an initial conversion price is $6.50 per share. The conversion rate is subject to adjustment in customary circumstances such as stock splits or similar changes to our capitalization. At our election, we may choose to make such conversion payment in cash, in shares of common stock, or in a combination thereof. Upon any conversion of any Convertible Note, we are obligated to make a cash payment to the holder of such Convertible Note for any interest accrued but unpaid on the principal amount converted. Upon the occurrence of a Corporate Transaction (as defined in the Convertible Notes), the holder of a Convertible Note is entitled, at such holder's option, to convert all of the outstanding principal amount of the Convertible Note in accordance with the foregoing and receive an additional, "make-whole" cash payment in accordance with a table set forth in each Convertible Note. Upon the occurrence of a Corporate Transaction, each holder of a Convertible Note has the option to require us to repurchase all or part of the outstanding principal amount of such Convertible Note at a repurchase price equal to 100% of the outstanding principal amount of the Convertible Note to be repurchased, plus accrued and unpaid interest to, but excluding, the repurchase date. If the last reported sale price of the common stock has been at least 130% of the conversion rate then in effect for twenty of the preceding thirty trading days (including the last trading day of such period), we are entitled, at our option, to redeem all or part of the outstanding principal amount of the Convertible Notes, on a pro rata basis, at an optional redemption price equal to 100% of the outstanding principal amount of the Convertible Notes to be redeemed, plus accrued and unpaid interest to, but excluding, the optional redemption date. The Purchase Agreement contains customary representations and warranties by us and the noteholder. The Purchase Agreement does not include any financial covenants. Our obligations under the Purchase Agreement and the Convertible Notes are subject to acceleration upon the occurrence of specified events of default, including a default or breach of certain contracts material to us and the delisting and deregistration of our common stock.

In connection with entering the Barings Credit Facility, in August 2023, we paid MidCap Financial Trust, as administrative agent, and our other lenders an aggregate of $26.2 million in satisfaction of our obligations under the MidCap Credit Facility.

2024 Private Placement

In February 2024, we sold 32,413,560 shares of our common stock at $7.52 per share and, in lieu of common stock to certain investors, pre-funded warrants to purchase up to an aggregate of 10,805,957 shares of our common stock at a price of $7.519 per pre-funded warrant for aggregate gross proceeds of approximately $325.0 million, before deducting placement agent fees and other offering expenses, under the 2024 Private Placement. Each pre-funded warrant has an exercise price of $0.001 per share, is currently exercisable and will remain exercisable until exercised in full.

Funding Requirements

We have a history of incurring significant operating losses. Our net losses were $80.7 million, $71.0 million, and $6.6 million for the years ended December 31, 2023, 2022 and 2021, respectively. As of December 31, 2023, we had an accumulated deficit of $697.6 million.

We expect to continue to incur losses in connection with our ongoing activities, particularly as we advance the clinical trials of our product candidates in development and increase our sales and marketing resources to support the commercialization of DEXTENZA and the potential launch of our product candidates, subject to receiving FDA approval.

We anticipate we will incur substantial expenses if and as we:

- continue our ongoing clinical trials, including the SOL-1 trial of AXPAXLI for the treatment of wet AMD; our Phase 1 clinical trials of AXPAXLI for the treatment of wet AMD; the HELIOS trial of AXPAXLI for the treatment of NPDR; our Phase 2 clinical trial of PAXTRAVA for the treatment of OAG or OHT; our Phase 2 clinical trial of OTX-DED for the short-term treatment of the signs and symptoms of dry eye disease;
- continue to monitor subjects according to the applicable clinical trial protocols in our clinical trials that have been completed, including our clinical trial to evaluate DEXTENZA in pediatric subjects following cataract surgery;
- determine to initiate new clinical trials to evaluate our product candidates, including our planned SOL-2 trial of AXPAXLI for the treatment of wet AMD; our planned pivotal clinical trials of AXPAXLI for the treatment of NPDR; and, subject to our evaluation of strategic alternatives, possible pivotal clinical trials of PAXTRAVA for the reduction of IOP in patients with primary OAG or OHT;
- continue to commercialize DEXTENZA in the United States;
- continue to develop and expand our sales, marketing and distribution capabilities for DEXTENZA and any other products or product candidates we intend to commercialize;
- conduct or support research and development activities on, and seek regulatory approvals for, DEXTENZA and PAXTRAVA in specified Asian markets pursuant to our license agreement and collaboration with AffaMed Therapeutics Limited, or AffaMed;
- continue the research and development of our other product candidates;
- seek to identify and develop additional product candidates;
- seek marketing approvals for any of our product candidates that successfully complete clinical development;
- scale up our manufacturing processes and capabilities to support sales of commercial products, clinical trials of our product candidates and commercialization of any of our product candidates for which we obtain marketing approval, and expand our facilities to accommodate this scale up and any corresponding growth in personnel;
- renovate our existing facilities including research and development laboratories, manufacturing space and office space;
- maintain, expand and protect our intellectual property portfolio;
- expand our operational, financial, administrative and management systems and personnel, including personnel to support our clinical development, manufacturing and commercialization efforts;
- defend ourselves against legal proceedings, if any;
- make investments to improve our defenses against cybersecurity and establish and maintain cybersecurity insurance;
- increase our product liability and clinical trial insurance coverage as we expand our clinical trials and commercialization efforts; and
- continue to operate as a public company.

The amount and timing of these expenses determines our future capital requirements.

Based on our current operating plan, which includes estimates of anticipated cash inflows from DEXTENZA product sales and cash outflows from operating expenses and capital expenditures and reflects our observance of the minimum liquidity covenant of $20.0 million under the Barings Credit Agreement, we believe that our existing cash and cash equivalents as of December 31, 2023, plus the cash received from the 2024 Private Placement of our common stock in February 2024 of $325.0 million before deducting placement agent fees and other offering expenses, will enable us to fund our planned operating expenses, debt service obligations and capital expenditure requirements at least into 2028. We have based our estimates on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect.

Our future capital requirements will depend on many factors, including:

- the level of product sales from DEXTENZA and any additional products for which we obtain marketing approval in the future and the level of third-party reimbursement of such products;
- the costs of sales, marketing, distribution and other commercialization efforts with respect to DEXTENZA and any additional products for which we obtain marketing approval in the future, including cost increases due to inflation;
- the progress, costs and outcome of our ongoing and planned clinical trials of our product candidates, in particular AXPAXLI for the treatment of wet AMD and NPDR, and, subject to our evaluation of strategic alternatives, PAXTRAVA for the treatment of OAG or OHT;
- the scope, progress, costs and outcome of preclinical development and clinical trials of our other product candidates;
- the costs, timing and outcome of regulatory review of our product candidates by the FDA, the EMA or other regulatory authorities;
- the costs of scaling up our manufacturing processes and capabilities to support sales of commercial products, clinical trials of our product candidates and commercialization of any of our product candidates for which we obtain marketing approval and of expanding our facilities to accommodate this scale up and any corresponding growth in personnel;
- the extent of our debt service obligations and our ability, if desired, to refinance any of our existing debt on terms that are more favorable to us;
- the amounts we are entitled to receive, if any, as reimbursements for clinical trial expenditures, development, regulatory, and sales milestone payments, and royalty payments under our license agreement with AffaMed;
- the extent to which we choose to establish additional collaboration, distribution or other marketing arrangements for our products and product candidates;
- the costs and outcomes of any legal actions and proceedings;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and
- the extent to which we acquire or invest in other businesses, products and technologies.

Until such time, if ever, as we can generate product revenues sufficient to achieve profitability, we expect to finance our cash needs through equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements, royalty agreements, and marketing and distribution arrangements. We do not have any committed external source of funds, although our license agreement with AffaMed provides for AffaMed's reimbursement of certain clinical expenses incurred by us in connection with our collaboration and for our potential receipt of development and sales milestone payments and royalty payments. To the extent that we raise additional capital through the sale of equity, preferred equity or convertible debt securities, our securityholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our existing securityholders' rights as holders or beneficial owners of our common stock. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Our pledge of our assets as collateral to secure our obligations under the Barings Credit Facility pursuant to which we have a total borrowing capacity of $82.5 million, which has been fully drawn down, may limit our ability to obtain additional debt or other financing. If we raise additional funds through collaborations, strategic alliances, licensing arrangements, royalty agreements or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, products or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

Cash Flows

The following table summarizes our sources and uses of cash for each of the periods presented:

	Year Ended December 31,		
	2023	2022	2021
		(in thousands)	
Cash used in operating activities	$ (70,234)	$ (59,603)	$ (65,550)
Cash used in investing activities	(6,087)	(3,715)	(1,194)
Cash provided by financing activities	169,828	1,454	2,851
Net increase (decrease) in cash and cash equivalents	$ 93,507	$ (61,864)	$ (63,893)

Operating activities.

Net cash used in operating activities was $70.2 million for the year ended December 31, 2023, primarily resulting from our net loss of $80.7 million, adjusted for net gains on extinguishment of debt of $14.2 million, partially offset by changes in the fair value of our derivative liabilities of $5.2 million and $19.5 million of other non-cash items and changes in operating assets and liabilities. Our net loss was primarily attributed to research and development activities, selling and marketing costs and our general and administrative expenses partially offset by $58.4 million of revenue and other income of $1.6 million. Our other non-cash items during the year ended December 31, 2023 consisted primarily of $17.8 million of stock-based compensation expense, $6.1 million in non-cash interest expense, and $3.0 million in depreciation and amortization expense, partially offset by $7.4 million unfavorable changes in our operating assets and liabilities. Net cash used by unfavorable changes in our operating assets and liabilities during the year ended December 31, 2023 consisted primarily of net increases of prepaid expenses and other current assets of $5.0 million, net increases in accounts receivable of $4.9 million, partially offset by increases of accounts payable, excluding accounts payable related to additions to property and equipment, of $1.8 million, and increases in accrued expenses and other current liabilities, excluding accrued non-cash interest, of $0.8 million.

Net cash used in operating activities was $59.6 million for the year ended December 31, 2022, primarily resulting from our net loss of $71.0 million, adjusted for changes in the fair value of our derivative liabilities of $13.8 million, partially offset by $25.2 million of other non-cash items and changes in operating assets and liabilities. Our net loss was primarily attributed to research and development activities, selling and marketing costs and our general and administrative expenses partially offset by $51.5 million of revenue and $7.6 million of other income. Our other non-cash items during the year ended December 31, 2022 consisted primarily of $17.0 million of stock-based compensation expense, $4.9 million in non-cash interest expense, $2.1 million in depreciation and amortization expense, and $1.3 million net cash generated by favorable changes in our operating assets and liabilities. Net cash generated by changes in our operating assets and liabilities during the year ended December 31, 2022 consisted primarily of an increase of $1.6 million in accrued expenses, an increase in deferred revenue of $1.0 million and a decrease of prepaid expenses of $0.7 million partially offset by increase in inventory of $0.7 million, decrease in accounts payable of $0.6 million and an increase of accounts receivable of $0.2 million.

Net cash used in operating activities was $65.6 million for the year ended December 31, 2021, primarily resulting from our net loss of $6.6 million, adjusted for changes in the fair value of our derivative liabilities of $78.1 million, partially offset by $19.1 million of other non-cash items and changes in operating assets and liabilities. Our net loss was primarily attributed to research and development activities, selling and marketing costs and our general and administrative expenses partially offset by $71.5 million of other income and $43.5 million of revenue. Our other non-cash items during the year ended December 31, 2021 consisted primarily of $15.0 million of stock-based compensation expense, $4.6 million in non-cash interest expense, and $2.4 million in depreciation and amortization expense, partially offset by $2.9 million unfavorable changes in our operating assets and liabilities. Net cash used by unfavorable changes in our operating assets and liabilities during the year ended December 31, 2021 consisted primarily of an increase of $8.9 million in accounts receivable, partially offset by increases in accrued expenses and other current liabilities, excluding accrued non-cash interest, of $3.7 million, increases of accounts payable, excluding accounts payable related to additions to property and equipment, of $1.8 million, and increases of deferred revenue of $1.0 million.

Investing activities. Net cash used in investing activities was $6.1 million for the year ended December 31, 2023, consisting of cash used to purchase property and equipment and leasehold improvements. Net cash used in investing activities was $3.7 million for the year ended December 31, 2022, consisting of cash used to purchase property and equipment. Net cash used in investing activities was $1.2 million for the year ended December 31, 2021, consisting of cash used to purchase property and equipment.

Financing activities. Net cash provided by financing activities for the year ended December 31, 2023 was $169.8 million and consisted of proceeds from the issuance of common stock in public offerings of $117.3 million, drawings under the Barings Credit Facility of $77.3 million, net of issuance costs, proceeds from the issuance of common stock pursuant to our employee stock purchase plan of $0.9 million and proceeds from the exercise of stock options of $0.6 million, partially offset by repayment of the MidCap Credit Facility of $26.1 million.

Net cash provided by financing activities for the year ended December 31, 2022 was $1.5 million and consisted of proceeds from the issuance of common stock pursuant to our employee stock purchase plan of $0.9 million and proceeds from the exercise of stock options of $0.5 million.

Net cash provided by financing activities for the year ended December 31, 2021 was $2.9 million and consisted primarily of $3.7 million, net, of proceeds in borrowings under our Credit Facility, proceeds from the exercise of stock options of $2.6 million; and proceeds from the issuance of common stock pursuant to our employee stock purchase plan of $1.0 million offset by payments on notes payable of $4.2 million.

Contractual Obligations and Commitments

	Total	Less Than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 Years
		(in thousands)			
Operating lease commitments	$ 10,713	$ 2,504	7,493	716	—
Barings Credit Agreement	82,474	—	—	—	82,474
Convertible Notes	61,535	—	—	—	61,535
Total	$ 154,722	$ 2,504	$ 7,493	$ 716	$ 144,009

The table above includes our enforceable and legally binding obligations and future commitments at December 31, 2023, as well as obligations related to contracts that we are likely to continue, regardless of the fact that they may be cancelable at December 31, 2023. Some of the figures that we include in this table are based on management's estimates and assumptions about these obligations, including their duration, and other factors. Because these estimates and assumptions are necessarily subjective, the amounts we will actually pay in future periods may vary from those reflected in the table.

We enter into contracts in the normal course of business to assist in the performance of our research and development activities and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore are cancelable contracts which are not included in contractual obligations and commitments.

Operating lease commitments represent payments due under our leases of office, laboratory and manufacturing space in Bedford, Massachusetts and certain office equipment under operating leases that expire in March 2024, July 2027, and July 2028.

The commitments under the Barings Credit Agreement represent repayment of principal only. Future payments of interest under the Barings Credit Agreement depends on the level of SOFR, and future payments of royalty fees depend on our future revenue from DEXTENZA, both of which cannot be estimated at this time.

The commitments under the Convertible Notes represent repayment of principal and payment of previously accrued interest at maturity in November 2029.

We have in-licensed a significant portion of our intellectual property from Incept, an intellectual property holding company, under an amended and restated license agreement, or the License Agreement, that we entered into with Incept in January 2012, which was most recently amended in September 2018. We are obligated to pay Incept a royalty equal to a low-single-digit percentage of net sales made by us or our affiliates of any products, devices, materials, or components thereof, or the Licensed Products, including or covered by Original IP (as defined in the License Agreement), excluding the Shape-Changing IP (as defined in the License Agreement), in the Ophthalmic Field of Use (as defined in the License Agreement). We are obligated to pay Incept a royalty equal to a mid-single-digit percentage of net sales made by us or our affiliates of any Licensed Products including or covered by Original IP, excluding the Shape-Changing IP, in the Additional Field of Use (as defined in the License Agreement). We are obligated to pay Incept a royalty equal to a low-single-digit percentage of net sales made by us or our affiliates of any Licensed Products including or covered by Incept IP (as defined in the License Agreement) or Joint IP (as defined in the License Agreement) in the field of drug delivery. Any sublicensee of ours also will be obligated to pay Incept a royalty on net sales of Licensed Products made by it and will be bound by the terms of the agreement to the same extent as we are. We are obligated to reimburse Incept for our share of the reasonable fees and costs incurred by Incept in connection with the prosecution of the patent applications licensed to us under the agreement. Our share of these fees and costs is equal to the total amount of such fees and costs divided by the total number of Incept's exclusive licensees of the patent application. We have not included in the table above any payments to Incept under this license agreement as the amount, timing and likelihood of such payments are not known.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the Securities and Exchange Commission, such relationships with unconsolidated entities or financial partnerships, which are often referred to as structured finance or special purpose entities, established for the purpose of facilitating financing transactions that are not required to be reflected on our balance sheets.

Critical Accounting Policies and Significant Judgments and Estimates

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

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this annual report, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Revenue Recognition

We recognize product revenue from the sales of DEXTENZA product.

In November 2018, the FDA approved DEXTENZA for the treatment of ocular pain following ophthalmic surgery. We entered into a limited number of arrangements with specialty distributors in the United States to distribute DEXTENZA. Accounting Standards Codification 606 – *Revenue from Contracts with Customers*, or Topic 606, applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance arrangements and financial instruments. Under Topic 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to be entitled to in exchange for those goods or services.

To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps: (i) identify the contract(s) with a customer, (ii) identify the performance obligations in the contract, (iii) determine the transaction price, (iv) allocate the transaction price to the performance obligations in the contract, and (v) recognize revenue when (or as) the entity satisfies a performance obligation. We only apply the five-step model to arrangements that meet the definition of a contract with a customer under Topic 606, including when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer. At contract inception, once the contract is determined to be within the scope of Topic 606, we assess the goods or services promised within each contract, determines those that are performance obligations, and assesses whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. For a complete discussion of accounting for product revenue, see *Product Revenue, Net* (below).

Product Revenue, Net— We derive our product revenues from the sale of DEXTENZA in the United States to customers, which includes a limited number of specialty distributors, who then subsequently resell DEXTENZA to physicians, clinics and certain medical centers or hospitals. We also sell DEXTENZA directly to a small population of ASCs, based on individually negotiated direct distribution agreements. In addition, we enter into arrangements with health care providers and payors that provide for government mandated or privately negotiated rebates and chargebacks with respect to the purchase of DEXTENZA.

We recognize revenue on product sales when the customer obtains control of our product, which occurs at a point in time (upon delivery to the customer). We have determined that the delivery of DEXTENZA to our customers constitutes a single performance obligation. There are no other promises to deliver goods or services beyond what is specified in each accepted customer order. We have assessed the existence of a significant financing component in the agreements with our customers. The trade payment terms with our customers do not exceed one year and therefore we have elected to apply the practical expedient and no amount of consideration has been allocated as a financing component. Product revenues are recorded net of applicable reserves for variable consideration, including discounts and allowances.

Transaction Price, including Variable Consideration— Revenues from product sales are recorded at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established. Components of variable consideration include trade discounts and allowances, product returns, government chargebacks, discounts and rebates, and other incentives, such as voluntary patient assistance, and other fee-for-service amounts that are detailed within contracts between us and our customers relating to our sale of DEXTENZA. These reserves, as detailed below, are based on the amounts earned, or to be claimed on the related sales, and are classified as reductions of accounts receivable or a current liability. These estimates take into consideration a range of possible outcomes which are probability-weighted in accordance with the expected value method in Topic 606 for relevant factors such as current contractual and statutory requirements, specific known market events and trends, industry data, and forecasted customer buying and payment patterns. Overall, these reserves reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the respective underlying contracts.

The amount of variable consideration which is included in the transaction price may be constrained, and is included in the net sales price, only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized under the contract will not occur in a future period. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from our original estimates, we will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Trade Discounts and Allowances—We compensate (through trade discounts and allowances) our customers for sales order management, data, and distribution services. However, we have determined such services received to date are not distinct from our sale of products to the customer and, therefore, these payments have been recorded as a reduction of revenue within the statement of operations and comprehensive loss, as well as a reduction to trade receivables, net on the consolidated balance sheets.

Product Returns— Consistent with industry practice, we generally offer customers a limited right of return for product that has been purchased from us in certain circumstances as further discussed below. We estimate the amount of our product sales that may be returned by our customers and record this estimate as a reduction of revenue in the period the related product revenue is recognized, as well as within accrued expenses and other current liabilities, in the accompanying consolidated balance sheets. We currently estimate product return reserves using available industry data and our own sales information, including our visibility into the inventory remaining in the distribution channel. We have received minimal returns to date and believe the returns of DEXTENZA will be minimal.

Government Chargebacks— Chargebacks for fees and discounts to qualified government healthcare providers represent the estimated obligations resulting from contractual commitments to sell products to qualified U.S. Department of Veterans Affairs hospitals and 340B entities at prices lower than the list prices charged to customers who directly purchase the product from us. The 340B Drug Discount Program is a U.S. federal government program created in 1992 that requires drug manufacturers to provide outpatient drugs to eligible health care organizations and covered entities at significantly reduced prices. Customers charge us for the difference between what they pay for the product and the statutory selling price to the qualified government entity. These allowances are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and trade receivables, net. Chargeback amounts are generally determined at the time of resale to the qualified government healthcare provider by customers, and we generally issue credits for such amounts within a few weeks of the customer's notification to us of the resale. Allowances for chargebacks consist of credits that we expect to issue for units that remain in the distribution channel inventories at each reporting period-end that we expect will be sold to qualified healthcare providers, and chargebacks that customers have claimed, but for which we have not yet issued a credit.

Government Rebates— We are subject to discount obligations under state Medicaid programs and Medicare. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included in accrued expenses and other current liabilities on the consolidated balance sheets. For Medicare, we also estimate the number of patients in the prescription drug coverage gap for whom we will owe an additional liability under the Medicare Part D program. For Medicaid programs, we estimate the portion of sales attributed to Medicaid patients and record a liability for the rebates to be paid to the respective state Medicaid programs. Our liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel inventories at the end of each reporting period.

Purchaser/Provider Discounts and Rebates—We offer rebate payments for which ASCs, HOPDs and other prescribers qualify by meeting quarterly purchase volumes of DEXTENZA under our volume-based rebate program. We calculate rebate payment amounts due under this program quarterly, based on actual qualifying purchases and apply a contractual discount rate. In the third quarter of 2022, we implemented a separate off-invoice discount, or OID, rebate program whereby end-users receive the discounted price immediately upon purchase, rather than having to wait until the end of the quarter for a rebate payment. The OID amounts are generally determined at the time of resale by specialty distributors, or SDs, or direct sales to ASCs by us. We generally issue credits for such amounts within a few weeks of the SD's notification to us of the resale. We include the OID on the invoice when we sell to an ASC directly. The calculation of the accrual for all rebates is based on an estimate of claims that we expect to receive associated with product that has been recognized as revenue but also remains in the distribution channel inventories at the end of each reporting period. The adjustments are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included as an accrued expenses and other current liabilities for volume-based rebates and as a reduction of accounts receivable for OID rebates.

Other Incentives— Other incentives which we offer include voluntary patient assistance programs, such as the co-pay assistance program, which are intended to provide financial assistance to qualified commercially-insured patients with prescription drug co-payments required by payors. The calculation of the accrual for co-pay assistance is based on an estimate of claims and the cost per claim that we expect to receive associated with product that has been recognized as revenue, but remains in the distribution channel inventories at the end of each reporting period. The adjustments are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included as accrued expenses and other current liabilities on the consolidated balance sheets.

Derivative Liabilities

The Convertible Notes allow the holders to convert all or part of the outstanding principal of their Convertible Notes into shares our common stock provided that no conversion results in a holder beneficially owning more than 19.99% of our issued and outstanding common stock. The entire embedded conversion option is required to be separated from the Convertible Notes and accounted for as a freestanding derivative instrument subject to derivative accounting. Therefore, the entire conversion option is bifurcated from the underlying debt instrument and accounted for and valued separately from the host instrument. The main input when determining the fair value of the Convertible Notes is the bond yield that pertains to the host instrument without the conversion option. The significant assumption used in determining the bond yield is the market yield movements of a comparable instrument issued as of the valuation date, which is assessed and updated each period. We measure the value of the embedded conversion option at its estimated fair value and recognize changes in the estimated fair value in other income (expense), net in the consolidated statements of operations and comprehensive loss during the period of change. The embedded conversion is recognized as a derivative liability in our consolidated balance sheet.

The Barings Credit Agreement contains an embedded obligation to pay the Royalty Fee, or the Royalty Fee Obligation, that meets the criteria to be bifurcated and accounted for separately from the Barings Credit Facility, or the Royalty Fee Derivative Liability. Royalty payments are estimated using a Monte Carlo simulation. The main inputs when determining the fair value of the Royalty Fee Derivative Liability are the amount and timing of our expected future revenue, the estimated volatility of these revenues, and the discount rate corresponding to the risk of revenue. We measure the value of the Royalty Fee Derivative Liability at its estimated fair value and recognize changes in the estimated fair value in other income (expense), net in the consolidated statements of operations and comprehensive loss during the period of change. The Royalty Fee Derivative Liability is recognized as a derivative liability in our consolidated balance sheet.

Recently Issued Accounting Pronouncements

Information regarding new accounting pronouncements is included in Note 2 – *Summary of Significant Accounting Policies* to the current period's consolidated financial statements.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We are exposed to market risk related to changes in interest rates. As of December 31, 2023, we had cash and cash equivalents of $195.8 million, which includes cash in operating bank accounts, and investments in money market funds. We have policies requiring us to invest in high-quality issuers, limit our exposure to any individual issuer, and ensure adequate liquidity. Our primary exposure to market risk related to our cash and cash equivalents is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term securities. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our portfolio.

We do not enter into financial instruments for trading or speculative purposes.

As of December 31, 2023, we had a secured term loan facility with a principal amount of $82.5 million under a credit and security agreement with Barings Finance LLC and the lenders party thereto, or the Barings Credit Agreement. Expected cash outflows from this financial instrument fluctuate based on changes in the Secured Overnight Financing Rate, or SOFR, which is, among other factors, affected by the general level of U.S. and international central bank interest rates. As of December 31, 2023, an immediate 100 basis point increase or decrease in the SOFR would not have a material effect on the anticipated cash outflows from this instrument.

We account for the obligation to pay royalty fees embedded in the Barings Credit Agreement as a separate financial instrument, measured at fair value, using a Monte Carlo simulation, which we refer to as the Royalty Fee

Derivative Liability. As of December 31, 2023, the Royalty Fee Derivative Liability was valued at $12.4 million. As of December 31, 2023, a 10% increase or decrease of the interest rate used in the valuation model would not have a material effect on the fair value of the Royalty Fee Derivative Liability. Changes of the fair value of the Royalty Fee Derivative Liability have no impact on anticipated cash outflows.

We account for the conversion option embedded in our unsecured senior subordinated convertible notes, or the Convertible Notes, as a separate financial instrument, measured at fair value, using a binomial lattice model, which we refer to as the Conversion Option Derivative Liability. As of December 31, 2023, the Conversion Option Derivative Liability was valued at $17.6 million. As of December 31, 2023, a 10% increase or decrease of the main inputs to the valuation model would not have a material effect on the fair value of the Conversion Option Derivative Liability. Changes of the fair value of the Conversion Option Derivative Liability have no impact on anticipated cash outflows.

Item 8. Financial Statements and Supplementary Data

Our consolidated financial statements, together with the report of our independent registered public accounting firm, appear on pages F-1 through F-33 of this Annual Report on Form 10-K.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2023. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or 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, including our Chief Executive Officer and Chief Financial Officer recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2023, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management’s Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting for Ocular Therapeutix, Inc. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act as a process designed by, or under the supervision of, the company’s principal executive and principal financial officers and effected by the company’s board of directors, management and other personnel, 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 and includes those policies and procedures that:

- Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the company;

- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and

- Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management, including our President and Chief Executive Officer and Chief Financial Officer, assessed the effectiveness of our internal control over financial reporting as of December 31, 2023. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in *Internal Control—Integrated Framework (2013)*. Based on that assessment, our management concluded that, as of December 31, 2023, our internal control over financial reporting was effective.

Changes in Internal Control Over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the three months ended December 31, 2023 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions That Prevent Inspections

Not Applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Directors and Executive Officers

The information required by this item will be set forth in our Proxy Statement for the 2024 Annual Meeting of Stockholders and is incorporated in this Annual Report on Form 10-K by reference.

Delinquent Section 16(a) Reports

The information required by this item will be set forth in our Proxy Statement for the 2024 Annual Meeting of Stockholders, if applicable, and is incorporated in this Annual Report on Form 10-K by reference.

Code of Ethics

We have adopted a code of business conduct and ethics that applies to our directors and officers (including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions) as well as our other employees. A copy of our code of business conduct and ethics is available on our website. We intend to post on our website all disclosures that are required by applicable law, the rules of the Securities and Exchange Commission or the Nasdaq Global Market concerning any amendment to, or waiver of, our code of business conduct and ethics.

Director Nominees

The information required by this item will be set forth in our Proxy Statement for the 2024 Annual Meeting of Stockholders and is incorporated in this Annual Report on Form 10-K by reference.

Audit Committee

We have separately designated a standing Audit Committee established in accordance with Section 3(a)(58)(A) of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Additional information regarding the Audit Committee that is required by this item will be set forth in our Proxy Statement for the 2024 Annual Meeting of Stockholders and is incorporated in this Annual Report on Form 10-K by reference.

Audit Committee Financial Expert

Our board of directors has determined that Merilee Raines qualifies as an “audit committee financial expert” as defined by Item 407(d)(5) of Regulation S-K of the Exchange Act and is “independent” under the rules of the Nasdaq Global Market.

Item 11. Executive Compensation

The information required by this item will be set forth in our Proxy Statement for the 2024 Annual Meeting of Stockholders and is incorporated in this Annual Report on Form 10-K by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this item will be set forth in our Proxy Statement for the 2024 Annual Meeting of Stockholders and is incorporated in this Annual Report on Form 10-K by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this item will be set forth in our Proxy Statement for the 2024 Annual Meeting of Stockholders and is incorporated in this Annual Report on Form 10-K by reference.

Item 14. Principal Accounting Fees and Services

The information required by this item will be set forth in our Proxy Statement for the 2024 Annual Meeting of Stockholders and is incorporated in this Annual Report on Form 10-K by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules

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

No financial statement schedules have been filed as part of this Annual Report on Form 10-K because they are not applicable, not required or because the information is otherwise included in our consolidated financial statements or notes thereto.

The exhibits filed as part of this Annual Report on Form 10-K are set forth on the Exhibit Index immediately following Item 16. The Exhibit Index is incorporated herein by reference.

Item 16. Form 10-K Summary

None.

EXHIBIT INDEX

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
3.1	Restated Certificate of Incorporation of the Registrant, as amended	10-Q	001-36554	8/9/2021	3.1	
3.2	Amended and Restated By-laws of the Registrant	8-K	001-36554	7/30/2014	3.2	
4.1	Specimen Stock Certificate evidencing the shares of common stock	S-1/A	333-196932	7/11/2014	4.1	
4.2	Registration Rights Agreement, dated as of March 1, 2019, by and among the Registrant and the Purchasers identified therein	10-K	001-36554	3/7/2019	4.2	
4.3	Registration Rights Agreement, dated as of February 21, 2024, by and among the Registrant and the other parties thereto	8-K	001-36554	2/22/2024	10.2	
4.4	Form of Pre-Funded Warrant	8-K	001-36554	2/22/2024	4.1	
4.5	Description of Securities Registered under Section 12 of the Exchange Act	10-K	001-36554	2/28/2022	4.3	
10.1+	2006 Stock Incentive Plan, as amended	S-1	333-196932	6/20/2014	10.1	
10.2+	Form of Stock Option Agreement under 2006 Stock Incentive Plan	S-1	333-196932	6/20/2014	10.2	
10.3+	Form of Restricted Stock Agreement under 2006 Stock Incentive Plan	S-1	333-196932	6/20/2014	10.3	
10.4+	2014 Stock Incentive Plan	S-1/A	333-196932	7/11/2014	10.4	
10.5+	Form of Incentive Stock Option Agreement under 2014 Stock Incentive Plan	S-1/A	333-196932	7/11/2014	10.5	
10.6+	Form of Non-statutory Stock Option Agreement under 2014 Stock Incentive Plan	S-1/A	333-196932	7/11/2014	10.6	
10.7+	Form of Restricted Stock Agreement under 2014 Stock Incentive Plan	S-1/A	333-196932	7/11/2014	10.7	
10.8+	2019 Inducement Stock Incentive Plan	10-Q	001-36554	11/12/2019	10.1	

Exhibit Number	Description of Exhibit	Incorporated by Reference Form	File Number	Date of Filing	Exhibit Number	Filed Herewith
10.9+	Amendment to 2019 Inducement Stock Incentive Plan	10-K	001-36554	3/11/2021	10.9	
10.10+	Amendment No. 2 to 2019 Inducement Stock Incentive Plan	8-K	001-36554	2/22/2024	10.5	
10.11+	Form of Non-statutory Stock Option Agreement under 2019 Inducement Stock Incentive Plan	10-Q	001-36554	11/12/2019	10.2	
10.12+	Form of Restricted Stock Unit Agreement under 2019 Inducement Stock Incentive Plan					X
10.13†	Amended and Restated License Agreement, dated January 27, 2012, between the Registrant and Incept LLC	S-1	333-196932	6/20/2014	10.8	
10.14	Lease Agreement dated September 2, 2009, by and between the Registrant and RAR2-Crosby Corporate Center QRS, Inc., as amended.	S-1	333-196932	6/20/2014	10.9	
10.15+	2014 Employee Stock Purchase Plan	S-1/A	333-196932	7/11/2014	10.10	
10.16+	Amendment No. 1 to Employee Stock Purchase Plan, effective October 4, 2023	10-Q	001-36554	11/7/2023	10.3	
10.17	Form of Indemnification Agreement by and between the Registrant and each of its directors and executive officers	S-1	333-196932	6/20/2014	10.12	
10.18	Lease Agreement dated June 17, 2016 between the WS NF 15 Crosby Drive, LLC and the Registrant	10-Q	001-36554	8/9/2016	10.1	
10.19	Open Market Sale Agreement, dated as of August 9, 2021, by and between the Registrant and Jefferies LLC	8-K	001-36554	8/9/2021	1.1	
10.20+	Employment Agreement, by and between the Registrant and Philip Strassburger, dated August 28, 2020	10-K	001-36554	3/11/2021	10.19	

Exhibit Number	Description of Exhibit	Incorporated by Reference Form	File Number	Date of Filing	Exhibit Number	Filed Herewith
10.21+	Employment Agreement, by and between the Registrant and Antony C. Mattessich, dated as of June 20, 2017	8-K	001-36554	6/22/2017	10.2	
10.22+	Amendment to Employment Agreement by and between the Registrant and Antony C. Mattessich, dated as of February 21, 2024	8-K	001-36554	2/22/2024	10.4	
10.23+	Non-Statutory Stock Option Agreement, by and between the Registrant and Antony C. Mattessich dated as of June 20, 2017	8-K	001-36554	6/22/2017	10.3	
10.24+	Employment Agreement, by and between the Registrant and Donald Notman, dated as of September 25, 2017	8-K	001-36554	9/25/2017	10.1	
10.25	Second Amendment to Lease, by and between the Registrant and CCC Investors LLC, dated October 10, 2017	8-K	001-36554	10/16/2017	10.1	
10.26	Third Amendment to Lease, by and between the Registrant and Cobalt PropCo 2020 LLC, dated June 30, 2023	8-K	001-36554	7/7/2023	10.1	
10.27†	Second Amended and Restated License Agreement, dated September 13, 2018, by and between the Registrant and Incept LLC	8-K	001-36554	9/19/2018	10.1	
10.28	Note Purchase Agreement (including Form of Senior Subordinated Convertible Notes), dated as of February 21, 2019, by and among the Registrant and the Purchasers listed therein	8-K	001-36554	2/22/2019	10.1	
10.29	Amendment No. 1 to Senior Subordinated Convertible Note, dated as of August 2, 2023, between the Registrant and the holders thereof	10-Q	001-36554	11/7/2023	10.2	
10.30	Securities Purchase Agreement, dated February 21, 2024, by and among the Registrant and the other parties thereto	8-K	001-36554	2/22/2024	10.1	

Exhibit Number	Description of Exhibit	Incorporated by Reference Form	File Number	Date of Filing	Exhibit Number	Filed Herewith
10.31	Sublease, dated as of April 4, 2019, by and among Ocular Therapeutix, Inc. and Holcim (US) Inc.	10-Q	001-36554	5/10/2019	10.4	
10.32*	License Agreement, by and between the Registrant and AffaMed Therapeutics Limited, dated as of October 29, 2020	10-Q	001-36554	11/5/2020	10.1	
10.33*	Supplement to License Agreement, by and between the Registrant and AffaMed Therapeutics Limited, dated as of January 18, 2021	10-K	001-36554	3/11/2021	10.36	
10.34	Credit and Security Agreement, dated August 2, 2023, by and among Barings Finance LLC, as administrative agent, the Registrant, and the Lenders listed therein	10-Q	001-36554	11/7/2023	10.1	
10.35+	2021 Stock Incentive Plan, as amended	10-Q	001-36554	8/7/2023	10.2	
10.36+	Form of Option Grant Agreement under 2021 Stock Incentive Plan	10-K	001-36554	2/28/2022	10.39	
10.37+	Form of Restricted Stock Unit Agreement under 2021 Stock Incentive Plan					X
10.38	Amendment No. 1 to License Agreement, by and between the Registrant and AffaMed Therapeutics (HK) Limited, dated as of October 28, 2021	10-K	001-36554	2/28/2022	10.41	
10.39+	Employment Agreement, by and between the Registrant and Rabia Ozden-Gurses, dated as of September 28, 2022	10-K	001-36554	3/6/2023	10.44	
10.40+	Employment Agreement, by and between the Registrant and Christopher White, dated as of October 13, 2022	10-K	001-36554	3/6/2023	10.45	
10.41+	Employment Agreement, by and between the Registrant and Dr. Pravin U. Dugel, dated as of February 21, 2024	8-K	001-36554	2/22/2024	10.3	

Exhibit Number	Description of Exhibit	Incorporated by Reference Form	File Number	Date of Filing	Exhibit Number	Filed Herewith
10.42+	Employment Agreement, by and between the Registrant and Dr. Sanjay Nayak, dated as of February 21, 2024					X
21.1	Subsidiaries of the Registrant					X
23.1	Consent of PricewaterhouseCoopers LLP					X
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended					X
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended					X
32.1	Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
32.2	Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
97.1	Ocular Therapeutix, Inc. Compensation Recovery Policy					X
101.INS	Inline XBRL Instance Document (the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document)					X
101.SCH	Inline XBRL Taxonomy Extension Schema Document					X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document					X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Database					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document					X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document					X
104	The cover page from this Annual Report on Form 10-K, formatted in Inline XBRL and contained in Exhibit 101					X

† Confidential treatment has been granted as to certain portions, which portions have been omitted and separately filed with the Securities and Exchange Commission.

\+ Management contract or compensatory plan or arrangement filed in response to Item 15(a)(3) of the Instructions to the Annual Report on Form 10-K.

* Certain portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) 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: March 11, 2024

OCULAR THERAPEUTIX, INC.

By: /s/ Donald Notman
Donald Notman
Chief Financial Officer
(Principal Financial and Accounting Officer)

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

Signature	Title	Date
/s/ Antony Mattessich Antony Mattessich	President, Chief Executive Officer and Director (Principal Executive Officer)	March 11, 2024
/s/ Donald Notman Donald Notman	Chief Financial Officer (Principal Financial and Accounting Officer)	March 11, 2024
/s/ Pravin Dugel, M.D. Pravin Dugel, M.D.	Executive Chairman of the Board of Directors	March 11, 2024
/s/ Adrienne Graves, Ph.D. Adrienne Graves, Ph.D.	Director	March 11, 2024
/s/ Seung Suh Hong, Ph.D. Seung Suh Hong, Ph.D.	Director	March 11, 2024
/s/ Richard L. Lindstrom, M.D. Richard L. Lindstrom, M.D.	Director	March 11, 2024
/s/ Merilee Raines Merilee Raines	Director	March 11, 2024
/s/ Charles Warden Charles Warden	Director	March 11, 2024
/s/ Leslie Williams Leslie Williams	Director	March 11, 2024

OCULAR THERAPEUTIX, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Ocular Therapeutix, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Ocular Therapeutix, Inc. and its subsidiaries (the “Company”) as of December 31, 2023 and 2022, and the related consolidated statements of operations and comprehensive loss, of changes in stockholders’ equity (deficit) and of cash flows for each of the three years in the period ended December 31, 2023, including the related notes (collectively referred to as the “consolidated financial statements”). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2023 and 2022, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2023 in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

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

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

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

Critical Audit Matters

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

Valuation of the Convertible Notes Derivative Liability

As described in Notes 2, 10, and 11 to the consolidated financial statements, the Company’s Convertible Notes Derivative Liability balance was $17.6 million as of December 31, 2023 and the change in fair value recorded in other income (expense), net was $(4.5) million for the year ended December 31, 2023. The Conversion Option Derivative Liability was recorded at fair value upon the issuance of the Convertible Notes and is subsequently remeasured to fair value at each reporting period. The Conversion Option Derivative Liability was initially valued and remeasured using a “with-and-without” method. The “with-and-without” methodology involves valuing the whole instrument on an as-is basis and then valuing the instrument without the embedded conversion option. The difference between the entire instrument with the embedded conversion option compared to the instrument without the embedded conversion option is the fair value of the derivative, recorded as the Conversion Option Derivative Liability. The fair value of the Convertible Notes with and without the conversion option is estimated using a binomial lattice approach. The main inputs to valuing the Convertible Notes with the conversion option as of December 31, 2023 include the Company's stock price on the valuation date, the expected annual volatility of the Company's stock and the bond yield. The significant assumption used in determining the bond yield is the market yield movements of a comparable instrument issued as of the valuation date, which is assessed and updated each period.

The principal considerations for our determination that performing procedures relating to the valuation of the derivative liability is a critical audit matter are the significant judgment by management to determine the fair value of the derivative liability using a binomial lattice approach; this in turn led to a high degree of auditor judgment, subjectivity, and effort in performing procedures and in evaluating the audit evidence obtained related to the valuation of the derivative liability and management's significant assumption related to market yield movements used in determining the bond yield input. In addition, the audit effort involved the use of professionals with specialized skill and knowledge.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included, among others (i) the involvement of professionals with specialized skill and knowledge to assist in developing an independent range of fair values for the derivative liability and (ii) comparing the independent estimate to management's fair value estimate to evaluate the reasonableness of management's estimate. Developing the independent estimate involved testing the completeness and accuracy of the inputs provided by management and evaluating the reasonableness of management's significant assumption related to market yield movements used in determining the bond yield by considering observable data.

/s/PricewaterhouseCoopers LLP
Boston, Massachusetts
March 11, 2024

We have served as the Company's auditor since 2008.

OCULAR THERAPEUTIX, INC.

CONSOLIDATED BALANCE SHEETS

(In thousands, except share and per share data)

	December 31, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 195,807	$ 102,300
Accounts receivable, net	26,179	21,325
Inventory	2,305	1,974
Restricted cash	150	—
Prepaid expenses and other current assets	7,794	4,028
Total current assets	232,235	129,627
Property and equipment, net	11,739	9,856
Restricted cash	1,614	1,764
Operating lease assets	6,472	8,042
Total assets	$ 252,060	$ 149,289
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 4,389	$ 5,123
Accrued expenses and other current liabilities	28,666	24,097
Deferred revenue	255	576
Operating lease liabilities	1,586	1,599
Total current liabilities	34,896	31,395
Other liabilities:		
Operating lease liabilities, net of current portion	6,878	8,678
Derivative liabilities	29,987	6,351
Deferred revenue, net of current portion	14,135	13,387
Notes payable, net	65,787	25,257
Other non-current liabilities	108	93
Convertible Notes, net	9,138	28,749
Total liabilities	160,929	113,910
Commitments and contingencies (Note 17)		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 5,000,000 shares authorized and no shares issued or outstanding at December 31, 2023 and December 31, 2022, respectively	—	—
Common stock, $0.0001 par value; 200,000,000 shares authorized and 114,963,193 and 77,201,819 shares issued and outstanding at December 31, 2023 and December 31, 2022, respectively	12	8
Additional paid-in capital	788,697	652,213
Accumulated deficit	(697,578)	(616,842)
Total stockholders' equity	91,131	35,379
Total liabilities and stockholders' equity	$ 252,060	$ 149,289

The accompanying notes are an integral part of these consolidated financial statements.

OCULAR THERAPEUTIX, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(In thousands, except share and per share data)

	Year Ended December 31,		
	2023	**2022**	**2021**
Revenue:			
Product revenue, net	$ 57,870	$ 50,457	$ 43,522
Collaboration revenue	573	1,037	—
Total revenue, net	58,443	51,494	43,522
Costs and operating expenses:			
Cost of product revenue	5,281	4,540	4,406
Research and development	61,055	53,462	50,083
Selling and marketing	40,549	39,922	35,190
General and administrative	33,940	32,224	31,880
Total costs and operating expenses	140,825	130,148	121,559
Loss from operations	(82,382)	(78,654)	(78,037)
Other income (expense):			
Interest income	3,983	798	33
Interest expense	(11,338)	(7,022)	(6,671)
Change in fair value of derivative liabilities	(5,188)	13,841	78,121
Gains and losses on extinguishment of debt, net	14,190	—	—
Other income (expense), net	(1)	(1)	1
Total other income, net	1,646	7,616	71,484
Net loss	$ (80,736)	$ (71,038)	$ (6,553)
Net loss per share, basic	$ (1.01)	$ (0.92)	$ (0.09)
Weighted average common shares outstanding, basic	79,827,362	76,875,035	76,392,870
Net loss per share, diluted	$ (1.02)	$ (0.97)	$ (0.98)
Weighted average common shares outstanding, diluted	85,596,594	82,644,267	82,162,102

The accompanying notes are an integral part of these consolidated financial statements.

OCULAR THERAPEUTIX, INC.

CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY (DEFICIT)

(In thousands, except share data)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Par Value			
Balances at December 31, 2020	75,996,732	8	615,338	(539,251)	76,095
Issuance of common stock upon exercise of stock options	598,923	—	2,586	—	2,586
Issuance of common stock in connection with employee stock purchase plan	124,548	—	985	—	985
Issuance of common stock upon cashless exercise of warrant	11,737	—	—	—	—
Common stock issuance costs	—	—	(91)	—	(91)
Stock-based compensation expense	—	—	14,977	—	14,977
Net loss	—	—	—	(6,553)	(6,553)
Balances at December 31, 2021	76,731,940	8	633,795	(545,804)	87,999
Issuance of common stock upon exercise of stock options	137,502	—	514	—	514
Issuance of common stock in connection with employee stock purchase plan	332,377	—	940	—	940
Stock-based compensation expense	—	—	16,964	—	16,964
Net loss	—	—	—	(71,038)	(71,038)
Balances at December 31, 2022	77,201,819	8	652,213	(616,842)	35,379
Issuance of common stock upon exercise of stock options	141,952	—	551	—	551
Issuance of common stock in connection with employee stock purchase plan	290,691	—	851	—	851
Issuance of common stock upon public offering, net of issuance costs	36,934,926	4	117,257	—	117,261
Issuance of common stock upon vesting of restricted stock units	393,805	—	—	—	—
Stock-based compensation expense	—	—	17,825	—	17,825
Net Loss	—	—	—	(80,736)	(80,736)
Balances at December 31, 2023	114,963,193	$ 12	$ 788,697	$ (697,578)	$ 91,131

The accompanying notes are an integral part of these consolidated financial statements.

OCULAR THERAPEUTIX, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(In thousands)

	Year Ended December 31,		
	2023	**2022**	**2021**
Cash flows from operating activities:			
Net loss	$ (80,736)	$ (71,038)	$ (6,553)
Adjustments to reconcile net loss to net cash used in operating activities			
Stock-based compensation expense	17,825	16,964	14,977
Non-cash interest expense	6,106	4,853	4,628
Change in fair value of derivative liabilities	5,188	(13,841)	(78,121)
Depreciation and amortization expense	2,983	2,109	2,421
Gains and losses on extinguishment of debt, net	(14,190)	—	—
Gain (loss) on disposal of property and equipment	1	1	(1)
Changes in operating assets and liabilities:			
Accounts receivable	(4,854)	(190)	(8,883)
Prepaid expenses and other current assets	(3,766)	723	(101)
Inventory	(331)	(724)	(49)
Accounts payable	583	(621)	1,796
Operating lease assets	1,570	(3,175)	977
Accrued expenses	773	1,644	3,717
Deferred revenue	427	963	1,000
Operating lease liabilities	(1,813)	2,729	(1,358)
Net cash used in operating activities	(70,234)	(59,603)	(65,550)
Cash flows from investing activities:			
Purchases of property and equipment	(6,087)	(3,715)	(1,194)
Net cash used in investing activities	(6,087)	(3,715)	(1,194)
Cash flows from financing activities:			
Proceeds from issuance of short-term bridge loan	2,000	—	—
Proceeds from issuance of Barings notes payable	82,474	—	—
Proceeds from issuance of notes payable, net	—	—	3,722
Proceeds from exercise of stock options	551	514	2,586
Proceeds from issuance of common stock pursuant to employee stock purchase plan	851	940	985
Payments of debt financing costs	(5,184)	—	—
Proceeds from issuance of common stock upon public offering, net of issuance costs	117,261	—	—
Issuance costs from the issuance of common stock upon public offering in prior period	—	—	(275)
Repayment of MidCap notes payable	(26,125)	—	—
Repayment of notes payable	—	—	(4,167)
Repayment of short-term bridge loan	(2,000)	—	—
Net cash provided by financing activities	169,828	1,454	2,851
Net increase (decrease) in cash, cash equivalents and restricted cash	93,507	(61,864)	(63,893)
Cash, cash equivalents and restricted cash at beginning of period	104,064	165,928	229,821
Cash, cash equivalents and restricted cash at end of period	$ 197,571	$ 104,064	$ 165,928
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 5,464	$ 2,147	$ 1,932
Supplemental disclosure of non-cash investing and financing activities:			
Additions to property and equipment included in accounts payable and accrued expenses	$ 16	$ 1,384	$ 181

The accompanying notes are an integral part of these consolidated financial statements.

OCULAR THERAPEUTIX, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

(Amounts in thousands, except share and per share data)

1. Nature of the Business and Basis of Presentation

Ocular Therapeutix, Inc. (the "Company") was incorporated on September 12, 2006 under the laws of the State of Delaware. The Company is a biopharmaceutical company committed to enhancing people's vision and quality of life through the development and commercialization of innovative therapies for diseases and conditions of the eye, with a specific focus on retinal disease. The Company's program for retinal disease is led by AXPAXLI (axitinib intravitreal implant, also known as OTX-TKI), which is based on its ELUTYX proprietary bioresorbable hydrogel-based formulation technology.

The Company is subject to risks common to companies in the biotechnology industry including, but not limited to, new technological innovations, protection of proprietary technology, dependence on key personnel, compliance with government regulations, regulatory approval and compliance, reimbursement, uncertainty of market acceptance of products and the need to obtain additional financing. Recently approved products will require significant sales, marketing and distribution support up to and including upon their launch. Product candidates currently under development will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval, prior to commercialization.

The Company is currently commercializing DEXTENZA (dexamethasone insert) 0.4mg, an intracanalicular insert for the treatment of post-surgical ocular inflammation and pain and for the treatment of ocular itching associated with allergic conjunctivitis, in the United States. The Company's most advanced product candidate, AXPAXLI, formerly referred to as OTX-TKI, is in Phase 3 clinical development; the Company's other advanced product candidates are in either Phase 1 or Phase 2 clinical development. There can be no assurance that the Company's research and development will be successfully completed, that adequate protection for the Company's intellectual property will be obtained, that any products developed will obtain necessary government regulatory approval and adequate reimbursement or that any approved products will be commercially viable. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will generate significant revenue from product sales. The Company operates in an environment of rapidly changing technology and substantial competition from pharmaceutical and biotechnology companies. In addition, the Company is dependent upon the services of its employees and consultants. The Company may not be able to generate significant revenue from sales of any product for several years, if at all. Accordingly, the Company will need to obtain additional capital to finance its operations.

The Company has incurred losses and negative cash flows from operations since its inception, and the Company expects to continue to generate operating losses and negative cash flows from operations in the foreseeable future. As of December 31, 2023, the Company had an accumulated deficit of $697,578. Based on its current operating plan which includes estimates of anticipated cash inflows from product sales and cash outflows from operating expenses and capital expenditures, the Company believes that its existing cash and cash equivalents of $195,807 as of December 31, 2023, plus the cash received from a private placement of the Company's common stock in February 2024 of $325,000 before deducting placement agent fees and other offering expenses, will enable it to fund its planned operating expenses, debt service obligations and capital expenditures at least through the next 12 months from the issuance date of these consolidated financial statements while the Company observes a minimum liquidity covenant of $20,000 in its credit facility (Note 9). The future viability of the Company beyond that point is dependent on the Company's ability to generate cash flows from the sale of DEXTENZA and raise additional capital to finance its operations. The Company will need to finance its operations through public or private securities offerings, debt financings, collaborations, strategic alliances, licensing agreements, royalty agreements, or marketing and distribution agreements. Although the Company has been successful in raising capital in the past, there is no assurance that it will be successful in obtaining such additional financing on terms acceptable to the Company, if at all. If the Company is unable to obtain funding, the Company could be forced to delay, reduce or eliminate some or all of its research and development programs for product candidates, product portfolio expansion or commercialization efforts, which could adversely affect its business prospects, or the Company may be unable to continue operations.

2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"). The accompanying consolidated financial statements reflect the operations of the Company and its wholly-owned subsidiaries. All intercompany accounts and transactions have been eliminated.

Use of Estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, and the reported amounts of revenues and expenses during the reporting periods. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the measurement and recognition of reserves for variable consideration related to product sales, revenue recognition related to a collaboration agreement that contains multiple promises, the fair value of derivatives, stock-based compensation, and realizability of net deferred tax assets. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Actual results could differ from the Company's estimates.

Cash Equivalents

The Company considers all short-term, highly liquid investments with original maturities of ninety days or less at date of purchase to be cash equivalents. Cash equivalents, which primarily consist of investments in money market funds, are stated at fair value.

Revenue Recognition

The Company recognizes revenue in accordance with Accounting Standards Codification ("ASC") Topic 606 – *Revenue from Contracts with Customers* ("ASC 606"). Under ASC 606, an entity recognizes revenue when a customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to be entitled to in exchange for those goods or services.

To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer, (ii) identify the performance obligations in the contract, (iii) determine the transaction price, (iv) allocate the transaction price to the performance obligations in the contract, and (v) recognize revenue when (or as) the entity satisfies a performance obligation. At contract inception, the Company assesses the goods or services promised within each contract, determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Product Revenue

The Company sells DEXTENZA in the United States primarily to a limited number of specialty distributors ("SDs") under individually negotiated distribution agreements. These customers then subsequently resell DEXTENZA to physicians, clinics and certain medical centers or hospitals. The Company also sells DEXTENZA directly to a small population of ambulatory surgery centers ("ASCs") based on individually negotiated direct distribution agreements (the "Direct Customers"). In addition, the Company enters into arrangements with health care providers and payors that provide for government mandated or privately negotiated rebates and chargebacks with respect to the purchase of DEXTENZA.

The Company recognizes revenue on product sales when the customer obtains control of the Company's product, which occurs at a point in time (upon delivery to the customer). Product revenues are recorded net of applicable reserves for variable consideration, including discounts and allowances.

Transaction Price, including Variable Consideration— Revenues from product sales are recorded net of off-invoice discounts and reserves which are established for our estimate of variable consideration. Components of variable consideration include trade discounts and allowances, product returns, government chargebacks, discounts and rebates, and other incentives, such as voluntary patient assistance, and other fee-for-service amounts that are detailed within contracts between the Company and its customers. These reserves, as detailed below, are based on the amounts earned, or to be claimed on the related sales, and are classified as reductions of accounts receivable or a current liability. These estimates take into consideration a range of possible outcomes which are probability-weighted in accordance with the expected value method in ASC 606 for relevant factors such as current contractual and statutory requirements, specific known market events and trends, industry data, and forecasted customer buying and payment patterns. Overall, these reserves reflect the Company’s best estimates of the amount of consideration to which it is entitled based on the terms of the respective underlying contracts.

The amount of variable consideration which is included in the transaction price may be constrained, and is included in the net sales price, only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized under the contract will not occur in a future period. Actual amounts of consideration ultimately received may differ from the Company’s estimates. If actual results in the future vary from the Company’s original estimates, the Company will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Trade Discounts and Allowances—The Company compensates (through trade discounts and allowances) its customers for sales order management, data, and distribution services. However, the Company has determined such services received to date are not distinct from the Company’s sale of products to the customer and, therefore, these payments have been recorded as a reduction of revenue within the statement of operations and comprehensive loss, as well as a reduction to accounts receivables, net on the consolidated balance sheets.

Product Returns— Consistent with industry practice, the Company generally offers customers a limited right of return for product that has been purchased from the Company based on the products expiration date. The Company estimates the amount of its product sales that may be returned by its customers and records this estimate as a reduction of revenue in the period the related product revenue is recognized, as well as within accrued expenses and other current liabilities, in the accompanying consolidated balance sheets. The Company currently estimates product return reserves using available industry data and its own sales information, including its visibility into the inventory remaining in the distribution channel.

Government Chargebacks— Chargebacks for fees and discounts to qualified government healthcare providers represent the estimated obligations resulting from contractual commitments to sell products to qualified U.S. Department of Veterans Affairs hospitals and entities that are subject to the U.S. federal government 340B Drug Discount Program at prices lower than the list prices charged to SDs and Direct Customers. Chargeback amounts are generally determined at the time of resale to the qualified government healthcare provider by SDs and Direct Customers, and the Company generally issues credits for such amounts within a few weeks of the customer’s notification to the Company of the resale. Allowance for chargebacks also consist of credits that the Company expects to issue for units that remain in the distribution channel inventories at each reporting period-end that the Company expects will be sold to qualified healthcare providers, and chargebacks that customers have claimed, but for which the Company has not yet issued a credit. These allowances are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and accounts receivables, net.

Government Rebates— The Company is subject to discount obligations under state Medicaid programs and Medicare. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included in accrued expenses and other current liabilities on the consolidated balance sheets. For Medicare, the Company also estimates the number of patients in the prescription drug coverage gap for whom the Company will owe an additional liability under the Medicare Part D program. For Medicaid programs, the Company estimates the portion of sales attributed to Medicaid patients and records a liability for the rebates to be paid to the respective state Medicaid programs. The Company’s liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel inventories at the end of each reporting period.

Purchaser/Provider Discounts and Rebates— The Company offers rebate payments for which ASCs, hospital out-patient departments and other prescribers qualify by meeting quarterly purchase volumes of DEXTENZA under the Company's volume-based rebate program. The Company calculates rebate payment amounts due under this program quarterly, based on actual qualifying purchases and applies a contractual discount rate. In the third quarter of 2022, the Company implemented a separate off-invoice discount ("OID") rebate program whereby end-users receive the discounted price immediately upon purchase, rather than having to wait until the end of the quarter for a rebate payment. The OID amounts are generally determined at the time of resale by SDs or direct sales to ASCs by the Company. The Company generally issues credits for such amounts within a few weeks of the SD's notification to the Company of the resale. The Company includes the OID on the invoice when it sells to an ASC directly. The calculation of the accrual for all rebates is based on an estimate of claims that the Company expects to receive associated with product that has been recognized as revenue but also remains in the distribution channel inventories at the end of each reporting period. The adjustments are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included as an accrued expenses and other current liabilities for volume-based rebates and as a reduction of accounts receivable for OID rebates.

Other Incentives— Other incentives which the Company offers include voluntary patient assistance programs, such as the co-pay assistance program, which are intended to provide financial assistance to qualified commercially-insured patients with prescription drug co-payments required by payors. The calculation of the accrual for co-pay assistance is based on an estimate of claims and the cost per claim that the Company expects to receive associated with product that has been recognized as revenue, but remains in the distribution channel inventories at the end of each reporting period. The adjustments are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included as an accrued expenses and other current liabilities on the consolidated balance sheets.

Collaboration Revenue

The Company evaluates contracts that contain multiple promises to determine which promises are distinct. Promises are considered to be distinct and therefore, accounted for as separate performance obligations, provided that: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer and (ii) the promise to transfer the good or service to the customer is separately identifiable from other promises in the contract. In assessing whether a promise is distinct, the Company considers factors such as whether: (i) the Company provides a significant service of integrating goods and/or services with other goods and/or services promised in the contract; (ii) one or more of the goods and/or services significantly modifies or customizes, or are significantly modified or customized by one or more of the other goods and/or services promised in the contract; and (iii) the goods and/or services are highly interdependent or highly interrelated. Individual goods or services (or bundles of goods and/or services) that meet both criteria for being distinct are accounted for as separate performance obligations. Promises that are not distinct at contract inception are combined and accounted for as a single performance obligation. Options to acquire additional goods and/or services are evaluated to determine if such option provides a material right to the customer that it would not have received without entering into the contract. If so, the option is accounted for as a separate performance obligation. If not, the option is considered a marketing offer which would be accounted for as a separate contract upon the customer's election.

The Company considers the existence of any significant financing component within its arrangements based on whether a substantive business purpose exists to support the payment structure other than to provide a significant benefit of financing. The Company measures the transaction price based on the amount of consideration to which the Company expects to be entitled in exchange for transferring the promised goods and/or services to the customer. The Company utilizes either the expected value method or the most likely amount method to estimate the amount of variable consideration, depending on which method is expected to better predict the amount of consideration to which the Company will be entitled. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. With respect to arrangements that include payments for a development or regulatory milestone payment, the Company evaluates whether the associated event is considered likely of achievement and estimates the amount to be included in the transaction price using the most likely amount method. Milestone payments that are not within the Company's control or the control of the licensee, such as those dependent upon receipt of regulatory approval, are not considered to be likely of achievement until the triggering event occurs. At the end of each reporting period, the Company re-evaluates the probability of achievement of each milestone and any related constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenue and net loss in the period of adjustment. For arrangements that include sales-based royalties, including milestone payments based upon the achievement of a certain level of product sales, wherein the license is deemed to be the sole or predominant item to which the payments relate, the Company recognizes revenue upon the later of: (i) when the related sales occur or (ii) when the performance obligation to which some or all of the payment has been allocated has been satisfied (or partially satisfied). Consideration that would be received for optional goods and/or services is excluded from the transaction price at contract inception.

Accounts Receivable

Accounts receivable arise from product sales and are recognized at the amounts invoiced to customers, net of applicable reserves for variable consideration. The Company analyzes the actual payment history of its customers, the aging of receivables, current customer-specific developments and economic trends to estimate the reserve for current expected credit losses.

Inventory

The Company values its inventories at the lower of cost or estimated net realizable value. Costs, which include amounts related to direct labor, materials and manufacturing overhead, are determined using standard costs, which approximate average cost. The Company performs an assessment of the recoverability of capitalized inventory during each reporting period, and it writes down any excess and obsolete inventories to their estimated realizable value in the period in which the impairment is first identified. Such impairment charges, should they occur, are recorded within cost of product revenue.

The Company capitalizes inventory costs associated with the Company’s products after regulatory approval when, based on management’s judgment, future commercialization is considered probable and the future economic benefit is expected to be realized. Inventory acquired prior to receipt of marketing approval of a product candidate is expensed as research and development expense as incurred. Inventory that can be used in either the production of clinical or commercial product is expensed as research and development expense when selected for use in a clinical manufacturing campaign. Inventory produced that will be used in promotional marketing campaigns is expensed to selling and marketing expense when it is selected for use in a marketing program.

Fair Value Measurements

Certain assets and liabilities are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices) such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

Derivative Instruments

The Company recognizes all derivative instruments as either assets or liabilities at fair value through profit or loss on the Company's consolidated balance sheet. Changes in the estimated fair value of derivative instruments are recognized in other income (expense), net in the consolidated statements of operations and comprehensive loss.

If the Company determines that a financial or non-financial contract, a 'host contract', includes implicit or explicit terms that affect the cash flows of the contract in a manner similar to a stand-alone derivative instrument, an 'embedded derivative', the Company analyzes whether to account for the embedded derivative separately. The Company accounts for an embedded derivative not separately from the host contract if it is clearly and closely related to the host contract or if the entire contract is measured at fair value through profit or loss. In other cases, the Company accounts for an embedded derivative separately.

The Company measures the value of embedded derivatives that are accounted for separately at their respective fair values and recognizes changes in the respective estimated fair values in other income (expense), net in the consolidated statements of operations and comprehensive loss during the period of change. Embedded derivatives that are accounted for separately are recognized as derivative liabilities in the Company's consolidated balance sheet.

The Convertible Notes, as discussed in Note 9, allow the holders to convert all or part of the outstanding principal of their Convertible Notes into shares of the Company's common stock provided that no conversion results in a holder beneficially owning more than 19.99% of the issued and outstanding common stock of the Company. The entire embedded conversion option is required to be separated from the Convertible Notes and accounted for as a freestanding derivative instrument subject to derivative accounting. The main input when determining the fair value of the Convertible Notes is the bond yield that pertains to the host instrument without the conversion option. The significant assumption used in determining the bond yield is the market yield movements of a comparable instrument issued as of the valuation date, which is assessed and updated each period. Therefore, the entire conversion option is bifurcated from the underlying debt instrument and accounted for and valued separately from the host instrument.

The Barings Credit Agreement, as discussed in Note 9, contains an embedded obligation to pay a royalty fee that meets the criteria to be bifurcated and accounted for separately from the Barings Credit Facility, as discussed in Note 9, subject to derivative accounting. The main inputs when determining the fair value of the derivative liability are the amount and timing of our expected future revenue, the estimated volatility of these revenues, and the discount rate corresponding to the risk of revenue.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation. Depreciation expense is recognized using the straight-line method over a three- to five-year estimated useful life. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the related asset. Expenditures for repairs and maintenance of assets are charged to expense as incurred. Upon retirement or sale, the cost and related accumulated depreciation of assets disposed of are removed from the accounts and any resulting gain or loss is included in loss from operations.

Leases

The Company determines whether an arrangement is or contains a lease at inception. Operating leases are recognized on the consolidated balance sheets as operating lease assets, current portion of lease liabilities and long-term lease liabilities. Operating lease assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. Operating lease liabilities and their corresponding operating lease assets are recorded based on the present value of lease payments over the expected remaining lease term. The operating lease assets also include any lease payments made and adjustments for prepayments and lease incentives. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilized its incremental borrowing rate, which is the rate incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment. Lease terms may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. The Company reassesses the lease term and remeasures the lease liability if triggering events occur. Lease expense for lease payments is recognized on a straight-line basis over the lease term.

Impairment of Long-Lived Assets

Long-lived assets consist of property and equipment and right-of-use assets. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends, and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset over its fair value, determined based on discounted cash flows. The Company has had no impairment triggers of long-lived assets.

Research and Development Costs

Research and development costs are expensed as incurred. Included in research and development expenses are salaries, stock-based compensation and benefits of employees and other operational costs related to the Company's research and development activities, including external costs of outside vendors engaged to conduct preclinical studies and clinical trials, manufacturing costs of the Company's products prior to regulatory approval, costs related to collaboration agreements and facility-related expenses.

The Company records accruals for estimated ongoing research and development costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies, including the phase or completion of events, invoices received, estimates provided by vendors, and contracted costs. Judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

Advertising Costs

Advertising costs are expensed as incurred.

Accounting for Stock-Based Compensation

The Company measures all stock options and other stock-based awards granted to employees, directors, and nonemployees at the fair value on the date of the grant. The fair value of the awards is recognized as expense, net of estimated forfeitures, over the requisite service period, which is generally the vesting period of the respective award. The straight-line method of expense recognition is applied to all awards with service-only conditions.

The Company recognizes compensation expense for only the portion of awards that are expected to vest. In developing a forfeiture rate estimate, the Company has considered its historical experience to estimate pre-vesting forfeitures for service-based awards. The impact of a forfeiture rate adjustment will be recognized in full in the period of adjustment, and if the actual forfeiture rate is materially different from the Company's estimate, the Company may be required to record adjustments to stock-based compensation expense in future periods.

Compensation cost related to shares purchased through the Company's employee stock purchase plan, which is considered compensatory, is based on the estimated fair value of the shares on the offering date, including consideration of the discount and the look-back period. The Company estimates the fair value of the shares using a Black-Scholes option pricing model. Compensation expense is recognized over the six-month withholding period prior to the purchase date.

The Company classifies stock-based compensation expense in its consolidated statement of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in the Company's tax returns. Deferred taxes are determined based on the difference between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect in the years in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense.

The Company accounts for uncertainty in income taxes recognized in the consolidated financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the consolidated financial statements. The amount of the benefit that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate.

Interest and penalties related to income taxes are recorded as part of the income tax provision.

Segment Data

The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions. The Company's singular focus is on advancing its bioresorbable hydrogel product candidates for the programed-release delivery of therapeutic agents, specifically for ophthalmology. All property and equipment, net and all operating lease assets are held in the United States. All product revenue, net is attributable to the United States. Collaboration revenue is attributable to a customer in China (Note 3).

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity that result from transactions and economic events other than those with stockholders. For the years ended December 31, 2023, 2022 and 2021, there were no items that gave rise to other comprehensive loss and therefore, there was no difference between net loss and comprehensive loss.

Net Loss Per Share

Basic net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted average number of shares of common stock outstanding for the period. Diluted net loss attributable to common stockholders is computed by adjusting net loss attributable to common stockholders to reallocate undistributed earnings based on the potential impact of dilutive securities, outstanding stock options and common stock warrants, except where the result would be anti-dilutive. Diluted net loss per share attributable to common stockholders is computed by dividing the diluted net loss attributable to common stockholders by the weighted average number of common shares outstanding for the period, including potential dilutive common shares assuming the dilutive effect of the conversion of convertible debt securities, the exercise of outstanding stock options and common stock warrants. In the diluted net loss per share calculation, net loss would also be adjusted for the elimination of interest expense on convertible debt securities and the mark-to-market gain or loss on bifurcated conversion options, if the impact was not anti-dilutive.

Recently Issued Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board ("FASB") and adopted by the Company as of the specified effective date. The Company believes that recently issued accounting pronouncements that are not yet effective will not have a material impact on our consolidated financial statements and disclosures.

3. Licensing Agreements and Deferred Revenue

Incept License Agreement (in-licensing)

On September 13, 2018, the Company entered into a second amended and restated license agreement with Incept, LLC ("Incept") to use and develop certain intellectual property (the "Incept License"). Under the Incept License, as amended and restated, the Company was granted a worldwide, perpetual, exclusive license to use specific Incept technology to develop and commercialize products that are delivered to or around the human eye for diagnostic, therapeutic or prophylactic purposes relating to ophthalmic diseases or conditions. The Company is obligated to pay low single-digit royalties on net sales of commercial products developed using the licensed technology, commencing with the date of the first commercial sale of such products and until the expiration of the last to expire of the patents covered by the license. Any of the Company's sublicensees also will be obligated to pay Incept a royalty equal to a low single-digit percentage of net sales made by it and will be bound by the terms of the agreement to the same extent as the Company. The Company is obligated to reimburse Incept for its share of the reasonable fees and costs incurred by Incept in connection with the prosecution of the patent applications licensed to the Company under the Incept License.

Royalties paid under this agreement related to product sales were $1,713, $1,466 and $1,333 for the years ended December 31, 2023, 2022 and 2021, respectively. Royalties have been charged to cost of product revenue.

AffaMed License Agreement (out-licensing)

On October 29, 2020, the Company entered into a license agreement ("License Agreement") with AffaMed Therapeutic Limited ("AffaMed") for the development and commercialization of the Company's DEXTENZA product regarding ocular inflammation and pain following cataract surgery and allergic conjunctivitis (collectively, the "DEXTENZA Field") and for the Company's PAXTRAVA, formerly known as OTX-TIC, product candidate (collectively with DEXTENZA, the "AffaMed Licensed Products") regarding open-angle glaucoma or ocular hypertension (collectively, the "TIC Field" and, with the DEXTENZA Field, each a "Field"), in each case in mainland China, Taiwan, Hong Kong, Macau, South Korea, and the countries of the Association of Southeast Asian Nations (collectively, the "Territories"). The Company retains development and commercialization rights for the AffaMed Licensed Products in the rest of the world.

Under the License Agreement, the Company received a non-refundable upfront payment of $12,000 in December 2020, a $1,000 milestone in the fourth quarter of 2021, a $2,000 clinical support payment in the second quarter of 2022, and a $1,000 milestone payment in the second quarter of 2023. The Company is also eligible to receive up to an additional $87,000 in aggregate upon the achievement of certain regulatory, development and commercial milestones. The Company is also entitled to receive tiered, escalating royalties on the net sales of the AffaMed Licensed Products ranging from a low-teen to low-twenties percentage. Royalties under the License Agreement are payable on an AffaMed Licensed Product-by-AffaMed Licensed Product and jurisdiction-by-jurisdiction basis and are subject to potential reductions in specified circumstances, subject to a specified floor.

Under the License Agreement, the Company is generally responsible for expenses related to the development of the AffaMed Licensed Products in the applicable Fields in the Territories, provided that AffaMed (i) reimburse the Company a low-teen percentage of expenses incurred in connection with certain clinical trials conducted by the Company and designed to support marketing approval of the AffaMed Licensed Product by the FDA or the European Medicines Agency ("Global Studies"); (ii) is solely responsible for expenses incurred in connection with territory-specific clinical trials that it conducts in furtherance of the development plan agreed between the parties in the applicable Fields in the Territories ("Local Studies"); and (iii) reimburse the Company in full for expenses incurred in connection with obtaining and maintaining regulatory approvals of the AffaMed Licensed Products in the applicable Fields in the Territories. In the event AffaMed declines to participate in a Global Study or to conduct a Local Study in any jurisdiction in which the Company determines to conduct such a study, the Company is relieved of its obligation to provide AffaMed clinical data from such study, other than safety data, unless AffaMed subsequently reimburses the Company in the amounts described above plus a prespecified premium.

The License Agreement expires upon the expiration of the last royalty term for the last AffaMed Licensed Product in any applicable Field in the Territories. Either party may, subject to specified cure periods, terminate the License Agreement in the event of the other party's uncured breach. Either party may also terminate the License Agreement under specified circumstances relating to the other party's insolvency. AffaMed has the right to terminate the License

Agreement at any time after completion of a Phase 3 clinical trial for PAXTRAVA for any or no reason upon providing the Company three months' notice. During an established period following its change of control or its entry into a global licensing agreement that includes the Territories with a third party, the Company has the option to terminate the License Agreement, subject to a specified notice period and the repayment of any costs and expenses incurred by AffaMed in connection with the License Agreement, including upfront and milestone payments AffaMed has previously paid to the Company, at a prespecified premium.

The Company concluded that AffaMed is a customer in this arrangement, and as such, the arrangement falls within the scope of the revenue recognition guidance in ASC 606.

At the inception of the License Agreement, the Company identified the following performance obligations in the agreement:

- the license, regulatory filings and manufacturing of DEXTENZA (the "DEXTENZA Field performance obligation");
- the license, regulatory filings and manufacturing for the Company's PAXTRAVA product candidate regarding open-angle glaucoma or ocular hypertension in the Territories (the "PAXTRAVA Field performance obligation");
- the conduct of a Phase 2 clinical trial of PAXTRAVA (the "Phase 2 Clinical Trial of PAXTRAVA performance obligation"); and
- obligations to participate on various joint research, development and project committees, which the Company has concluded is not a material performance obligation.

The transaction price was allocated to the performance obligations based on the relative estimated standalone selling prices of each performance obligation.

The Company developed the estimated standalone selling price for the services and/or manufacturing and supply included in each of the performance obligations, as applicable, primarily based on the nature of the services to be performed and/or goods to be manufactured and estimates of the associated costs, adjusted for a reasonable profit margin that would be expected to be realized under similar contracts.

The Company has determined that any sales-based royalties and milestones will be recognized as the Company delivers the clinical and commercial manufactured product to AffaMed. Any changes in estimates may result in a cumulative catch-up based on the number of units of manufactured product delivered.

As of December 31, 2023, the transaction price was determined to be $16,000. All potential regulatory, development and commercial milestone payments in the amount of $87,000 did not meet the recognition criteria under the most likely method, because their achievement was highly dependent on factors outside the control of the Company and therefore, were excluded from the transaction price as of December 31, 2023. Furthermore, under the expected value method the Company excluded the potential royalties from the transaction price.

We recognize revenue related to the amounts allocated to the DEXTENZA Field performance obligation and the PAXTRAVA Field performance obligation based on the point in time upon which control of supply is transferred to AffaMed for each delivery of the associated supply. The Company currently expects to recognize the revenue over a period of approximately seven to eight years commencing on the date the Company begins delivering product to AffaMed. This estimate of this period considers the timing of development and commercial activities under the License Agreement and may be reduced or increased based on the various activities as directed by the joint committees, decisions made by AffaMed, regulatory feedback or other factors not currently known.

The Company recognized $573, $1,037 and $0 of collaboration revenue related to the Phase 2 Clinical Trial of PAXTRAVA performance obligation for the years ended December 31, 2023, 2022 and 2021, respectively.

As of December 31, 2023, the aggregate amount of the transaction price allocated to the partially unsatisfied Phase 2 Clinical Trial of PAXTRAVA performance obligation was $390. This amount is expected to be recognized as this performance obligation is satisfied through June 2025.

Deferred revenue activity for the year ended December 31, 2023 was as follows:

	Deferred Revenue
Deferred revenue at December 31, 2022	$ 13,963
Additions	1,000
Amounts recognized into revenue	(573)
Deferred revenue at December 31, 2023	$ 14,390

Regeneron Collaboration Agreement

On October 10, 2016, the Company entered into a Collaboration, Option and License Agreement (the “Regeneron Collaboration Agreement”) with Regeneron Pharmaceuticals, Inc. (“Regeneron”) for the development and potential commercialization of products using the Company’s hydrogel in combination with Regeneron’s large molecule VEGF-targeting compounds for the treatment of retinal diseases.

Under the terms of the Collaboration Agreement, the Company and Regeneron had agreed to conduct a joint research program with the aim of developing a sustained-release formulation of aflibercept, currently marketed under the tradename Eylea, that is suitable for advancement into clinical development. The Company had granted Regeneron an option (the “Option”) to enter into an exclusive, worldwide license to develop and commercialize products using the Company’s hydrogel in combination with Regeneron’s large molecule VEGF-targeting compounds (“Licensed Products”). Under the term of the Collaboration Agreement, Regeneron was responsible for funding an initial preclinical tolerability study. The Regeneron Collaboration Agreement was subsequently amended on May 8, 2020 (the “Regeneron Amendment”). Pursuant to the Regeneron Amendment, the Company and Regeneron had adopted a new work plan to transition joint efforts under the Regeneron Collaboration Agreement to the research and development of an extended-delivery formulation of aflibercept to be delivered to the suprachoroidal space. Regeneron had agreed to pay personnel and material costs of the Company for specified preclinical development activities in connection with the revised work plan, as well as certain other costs. In addition, the Regeneron Amendment provided for the modification of the terms of the Option previously granted to Regeneron under the Regeneron Collaboration Agreement. As amended, the Option was exclusive for twenty-four months following May 8, 2020. On August 5, 2021, Regeneron notified the Company of its termination of the Regeneron Collaboration Agreement, as amended. The termination became effective immediately.

In connection with the termination of the Regeneron Collaboration Agreement, all licenses, options and other rights granted to either party under the Regeneron Collaboration Agreement automatically terminated, other than the surviving joint intellectual property rights described below. The Company and Regeneron also became obligated to undertake certain transition activities upon the termination, including the return of specified property of the other party. Each party retains an equal, undivided ownership interest, which may be transferred, licensed and otherwise exploited without a duty to account to the other party, in certain intellectual property rights jointly developed under the collaboration.

As a result of the termination, the Company is no longer eligible to receive (i) reimbursement from Regeneron for ongoing research and development activities, (ii) a fee upon exercise of the Option, (iii) payments upon the achievement of specified development and regulatory milestones of the Regeneron Licensed Products, or (iv) tiered, escalating royalties in a range from a high-single digit to a low-to-mid teen percentage of net sales of Regeneron Licensed Products, in each case pursuant to the Regeneron Collaboration Agreement. The Company is also no longer obligated to reimburse Regeneron for certain development costs, up to an aggregate amount of $30,000 in certain circumstances, were Regeneron to have exercised the Option.

For the years ended December 31, 2023, 2022 and 2021, the Company had recorded $0, $0 and $768 related to work performed for preclinical development activities in connection with the revised work plan which the Company has recorded as a reduction of research and development expense as this research is not an output of the Company’s ordinary business activities. As of December 31, 2023 and 2022, the Company had not recorded any assets or liabilities with regard to the Regeneron Collaboration Agreement.

4. Cash Equivalents and Restricted Cash

The Company's statements of cash flows include restricted cash with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on such statements. A reconciliation of the cash, cash equivalents, and restricted cash reported within the balance sheet that sum to the total of the same amounts shown in the statement of cash flows is as follows:

	December 31, 2023	December 31, 2022	December 31, 2021
Cash and cash equivalents	$ 195,807	$ 102,300	$ 164,164
Restricted cash (current)	150	—	—
Restricted cash (non-current)	1,614	1,764	1,764
Total cash, cash equivalents and restricted cash as shown on the statements of cash flows	$ 197,571	$ 104,064	$ 165,928

The Company held restricted cash as security deposits for its real estate leases.

5. Inventory

Inventory consisted of the following:

	December 31, 2023	December 31, 2022
Raw materials	$ 302	$ 309
Work-in-process	1,012	899
Finished goods	991	766
	$ 2,305	$ 1,974

6. Property and Equipment, net

Property and equipment, net consisted of the following:

	December 31, 2023	December 31, 2022
Equipment	$ 15,515	$ 12,485
Leasehold improvements	14,699	9,074
Furniture and fixtures	1,268	1,268
Software	236	236
Construction in progress	281	4,071
	31,999	27,134
Less: Accumulated depreciation and amortization	(20,260)	(17,278)
	$ 11,739	$ 9,856

Depreciation and amortization expense was $2,983, $2,109 and $2,421 for the years ended December 31, 2023, 2022 and 2021, respectively.

7. Leases

The Company leases real estate, including laboratory, manufacturing and office space. The Company's leases have remaining lease terms ranging from less than 1 year to approximately 4.5 years. All of the Company's leases qualify as operating leases.

The lease for the Company's 20,445 square feet of manufacturing space located at 36 Crosby Drive in Bedford, Massachusetts commenced on June 30, 2018. On October 18, 2022, the Company exercised its option to extend the lease agreement by an additional five-year term, resulting in a new expiration date of July 31, 2028. Under the terms of the existing lease, rent for the five-year extension period was based on the current fair market rent for comparable space in the building and in other similar buildings in the same rental market as of August 1, 2023, the commencement date of the additional five-year term. The Company estimated the prevailing market rental rates at the time when the Company exercised the renewal option and included these in the remeasurement of the operating lease asset and the lease liability. This resulted in an increase of the operating lease assets and operating lease liabilities of $4,284 as of the remeasurement date. As this is an estimate for variable payments that depend on an index or a rate, the Company has not remeasured the payments for the five-year renewal period as of the commencement date of the five-year extension term. On June 30, 2023, the Company and the landlord executed an amendment to this lease, formally extending the term of the lease through July 31, 2028. This lease does not include any additional renewal options.

The lease is for approximately 70,712 square feet of general office, research and development and manufacturing space located at 15 Crosby Drive in Bedford, Massachusetts. The lease term commenced on February 1, 2017 and will expire on July 31, 2027. The Company has the option to extend the lease for two additional periods of five years each by delivering written notice of the exercise not earlier than fifteen months nor later than 12 months before expiration of the original term.

The lease for 30,036 square feet of office space located at 24 Crosby Drive in Bedford, Massachusetts commenced on April 18, 2019 and terminates on March 31, 2024 and does not include any lease renewal options.

Recognized lease costs were as follows:

	For the Year Ended December 31, 2023	For the Year Ended December 31, 2022	For the Year Ended December 31, 2021
Operating lease costs	$ 2,663	$ 2,369	$ 2,482
Variable lease costs	987	756	629
Total lease costs	$ 3,650	$ 3,125	$ 3,111

The minimum lease payments for the next five years and thereafter are expected to be as follows:

Year Ending December 31,	December 31, 2023
2024	2,504
2025	2,673
2026	2,709
2027	2,111
2028	716
Thereafter	—
Total lease payments	$ 10,713
Less: interest	2,249
Present value of operating lease liabilities	$ 8,464

The following table summarizes the weighted average remaining lease term and the weighted average incremental borrowing rate used to determine the operating lease liability:

	December 31, 2023	December 31, 2022
Weighted average remaining lease term in years	4.1	4.9
Weighted average discount rate	12.00 %	13.41 %

Supplemental disclosure of cash flow information related to the Company's operating leases included in cash flows provided by operating activities in its consolidated statements of cash flows is as follows:

	For the Year Ended December 31, 2023	For the Year Ended December 31, 2022	For the Year Ended December 31, 2021
Cash paid for amounts included in the measurement of lease liabilities	$ 2,663	$ 2,549	$ 2,482

8. Expenses

The Company recognized $880, $1,166, and $1,925 of advertising expenses for the years ended December 31, 2023, 2022 and 2021, respectively.

Accrued expenses consisted of the following:

	December 31, 2023	December 31, 2022
Accrued interest payable on Convertible Notes (Note 9)	10,886	8,756
Accrued payroll and related expenses	$ 8,156	$ 7,509
Accrued rebates and programs	5,117	3,560
Accrued research and development expenses	1,488	1,816
Accrued interest payable on Barings Credit Facility (Note 9)	803	—
Accrued professional fees	691	1,228
Accrued other	1,525	1,228
	$ 28,666	$ 24,097

9. Financial Liabilities

Barings Credit Agreement

On August 2, 2023 (the "Closing Date"), the Company entered into a credit and security agreement (the "Barings Credit Agreement") with Barings Finance LLC ("Barings"), as administrative agent, and the lenders party thereto, providing for a secured term loan facility for the Company (the "Barings Credit Facility") in the aggregate principal amount of $82,474 (the "Total Credit Facility Amount"). The Company borrowed the full amount of $82,474 at closing and received proceeds of $77,290, after the application of an original issue discount and fees. Indebtedness under the Barings Credit Facility matures on the earlier to occur of (i) the six-year anniversary of the Closing Date and (ii) the date that is 91 days prior to the maturity date for the Company's Convertible Notes (as defined below). Indebtedness under the Barings Credit Facility incurs interest based on the Secured Overnight Financing Rate ("SOFR"), subject to a minimum 1.50% floor, plus 6.75%. The Company is obligated to make interest payments on its indebtedness under the Barings Credit Facility on a monthly basis, commencing on the Closing Date; to pay annual administration fees; and to pay, on the maturity date, any principal and accrued interest that remains outstanding as of such date. In addition, the Company is obligated to pay a fee in an amount equal to the Total Credit Facility Amount, which amount shall be reduced by the total amount of interest and principal prepayment fees paid under the Barings Credit Agreement (such fee, the "Barings Royalty Fee"). The Company is required to pay the Barings Royalty Fee in installments to Barings, for the benefit of the lenders, on a quarterly basis in an amount equal to three and one-half percent (3.5%) of the net sales of DEXTENZA occurring during such quarter, subject to the terms, conditions and limitations specified in the Barings Credit Agreement, until the Barings Royalty Fee is paid in full. The Barings Royalty Fee is due and payable upon a change of control of the Company. In the event the Company completes a change of control transaction or a sale of all or substantially all of its assets on or prior to the twelve-month anniversary of the Closing Date, the Barings Royalty Fee is subject to a reduction to an amount that is equal to (i) 20% of the Total Credit Facility Amount, in the event that a signed letter of intent evidencing such transaction was entered into by the Company on or prior to the date that is six months after the Closing Date and (ii) 30% of the Total Credit Facility Amount, in the event that a signed letter of intent evidencing such transaction was entered into by the Company after the date that is six months, but before the date that is twelve months, after the Closing Date. The Company may, at its option, prepay any or all of the Barings Royalty Fee at any time without penalty. In connection with the Barings Credit Agreement, the Company granted the lenders thereto a first-priority security interest in all assets of the Company, including its intellectual property, subject to certain agreed-upon exceptions. The Barings Credit Agreement includes negative covenants restricting the Company from making payments to the holders of the Convertible Notes, except in connection with a proposed conversion to equity and with respect to certain permitted expenses and requiring the Company to maintain a minimum liquidity amount of $20,000. The Barings Credit Agreement also includes customary affirmative and negative covenants.

The Company determined that the embedded obligation to pay the Barings Royalty Fee (the "Barings Royalty Fee Obligation") is required to be separated from the Barings Credit Facility and accounted for as a freestanding derivative instrument subject to derivative accounting. The allocation of proceeds to the Barings Royalty Fee Obligation resulted in a discount on the Barings Credit Facility. The Company is amortizing the discount to interest expense over the term of the Barings Credit Facility using the effective interest method. Accrued or paid Barings Royalty Fees are included in the change in fair value of derivative liabilities on the consolidated statements of operations and comprehensive loss. For the year ended December 31, 2023, Barings Royalty Fees were $901.

A summary of the Barings Credit Facility at December 31, 2023 is as follows:

	December 31, 2023
Barings Credit Facility	$ 82,474
Less: unamortized discount	(16,687)
Total	$ 65,787

As of December 31, 2023, the full principal for the Barings Credit Facility of $82,474 was due for repayment in 2029.

Convertible Notes

On March 1, 2019, the Company issued $37,500 of convertible notes which accrue interest at an annual rate of 6% of their outstanding principal amount, which is payable, along with the principal amount at maturity, unless earlier converted, repurchased or redeemed (as amended the "Convertible Notes").

Concurrently with entering into the Barings Credit Agreement, on August 2, 2023, the Company and the holders of the Convertible Notes extended the maturity of the Convertible Notes, which would otherwise have matured on March 1, 2026, to a date 91 days following the maturity of the indebtedness under the Barings Credit Facility, unless earlier converted, repurchased or redeemed (the "Amendment"). The Company accounted for the Amendment as an extinguishment of debt in accordance with the guidance in Accounting Standards Codification Topic 470-50 *Debt* ("ASC 470-50") and derecognized all liabilities related to the Convertible Notes, including the outstanding principal less unamortized discount, a derivative liability, and accrued interest, with a total carrying value of $51,090 as of the date of the Amendment. The Company determined that, after the Amendment, the embedded conversion option continues to be required to be separated from the Convertible Notes and accounted for the embedded conversion option as a freestanding derivative instrument subject to derivative accounting (the "Conversion Option Derivative Liability"). The total fair value of the Convertible Notes on August 2, 2023 after the Amendment, including the conversion option, was $36,183. The Company recognized the Convertible Notes and the Conversion Option Derivative Liability after the Amendment at their fair values as of the date of the Amendment of $18,482 and $17,701, respectively. A portion of the fair value of the Convertible Notes as of the date of the Amendment of $9,943 is presented in accrued expenses and other current liabilities on the consolidated balance sheets because the Convertible Notes are currently convertible, and this amount represents interest that was accrued before the Amendment and that would be payable in cash upon conversion. The allocation of a portion of the total fair value of the Convertible Notes to the Conversion Option Derivative Liability results in a discount on the Convertible Notes. Application of ASC 470-50 resulted in a gain on extinguishment of $14,907, which was charged to gains and losses on extinguishment of debt, net on the consolidated statements of operations and comprehensive loss for the year ended December 31, 2023.

The holders of the Convertible Notes may convert all or part of the outstanding principal amount of their Convertible Notes into shares of the Company's common stock, par value $0.0001 per share, prior to maturity and provided that no conversion results in a holder beneficially owning more than 19.99% of the issued and outstanding common stock of the Company. The conversion rate is initially 153.8462 shares of the Company's common stock per $1,000 principal amount of the Convertible Notes, which is equivalent to an initial conversion price of $6.50 per share.

The conversion rate is subject to adjustment in customary circumstances such as stock splits or similar changes to the Company's capitalization.

Upon conversion by the holder, other than a conversion based on a Corporate Transactions as defined below, the Company has the right to select the settlement of the conversion in either shares of common stock, cash, or in a combination thereof. Upon any conversion of any Convertible Note, the Company is obligated to make a cash payment to the holder of such Convertible Note for any interest accrued but unpaid on the principal amount converted.

- If the Company elects to satisfy such conversion by shares of common stock, the Company shall deliver to the converting holder in respect of each $1,000 principal amount of Convertible Notes being converted a number of common shares equal to the conversion rate in effect on the conversion date;

- If the Company elects to satisfy such conversion by cash settlement, the Company shall pay to the converting holder in respect of each $1,000 principal amount of Convertible Notes being converted cash in an amount equal to the sum of the Daily Conversion Values (as defined below) for each of the twenty (20) consecutive trading days during a specified period. The "Daily Conversion Values" is defined as each of the 20 consecutive trading days during the specified period, 5.0% of the product of (a) the conversion rate on such trading day and (b) the "Daily VWAP" on such trading day. The Daily VWAP is defined as each of the 20 consecutive trading days during the applicable Observation Period, the per share volume-weighted average price as displayed under the heading "Bloomberg VWAP" on the Bloomberg page for the Company.

- If the Company elects to satisfy such conversion by combination, the Company shall pay or deliver, as the case may be, in respect of each $1,000 principal amount of Convertible Notes being converted, a settlement amount equal to the sum of the "Daily Settlement Amounts" (as defined below) for each of the twenty (20) consecutive trading days during the specified period. The "Daily Settlement Amount" is defined as, for each of the 20 consecutive trading days during the specified period: (a) cash in an amount equal to the lesser of (i) the Daily Measurement Value (as defined below) and (ii) the Daily Conversion Value on such Trading Day; and (b) if the Daily Conversion Value on such trading day exceeds the Daily Measurement Value, a number of Shares equal to (i) the difference between the Daily Conversion Value and the Daily Measurement Value, divided by (ii) the Daily VWAP for such Trading Day. The "Daily Measurement Value" is defined as the Specified Dollar Amount (as defined below), if any, divided by 20. The "Specified Dollar Amount" is defined as the maximum cash amount per $1,000 principal amount of Notes to be received upon conversion as specified in the notice specifying the Company's chosen settlement method.

In the event of a Corporate Transaction, the noteholder shall have the right to either (a) convert all of the unpaid principal at the conversion rate and receive a cash payment equal to (i) the outstanding accrued but unpaid interest under the Convertible Note to, but excluding, the corporate transaction conversion date (to the extent such date occurs prior to a date 91 days following the maturity of the indebtedness under the Barings Credit Facility, the maturity date of the Convertible Notes) plus (ii) and an additional amount of consideration based on a sliding scale depending on the date of such as Corporate transaction or (b) require the Company to repurchase all or part of the outstanding principal amount of such Convertible Note at a repurchase price equal to 100% of the outstanding principal amount of the Convertible Note to be repurchased, plus accrued and unpaid interest to, but excluding, the repurchase date.

A corporate transaction includes (i) a merger or consolidation executed through a tender offer or change of control (other than one in which stockholders of the Company own a majority by voting power of the outstanding shares of the surviving or acquiring corporation); (ii) a sale, lease, transfer, of all or substantially all of the assets of the Company; or (iii) if the Company's common stock ceases to be listed or quoted on any of the New York Stock Exchange, the Nasdaq Global Select Market, the Nasdaq Global Market or the Nasdaq Capital Market (the "Corporate Transaction").

If the last reported sale price of the common stock has been at least 130% of the conversion rate then in effect for 20 of the preceding 30 trading days (including the last trading day of such period), the Company is entitled, at its option, to redeem all or part of the outstanding principal amount of the Convertible Notes, on a pro rata basis, at an optional redemption price equal to 100% of the outstanding principal amount of the Convertible Notes to be redeemed, plus accrued and unpaid interest to, but excluding, the optional redemption date.

The Convertible Notes are subject to acceleration upon the occurrence of specified events of default, including a default or breach of certain contracts material to the Company and the delisting and deregistration of the Company's common stock.

The Company determined that the embedded conversion option is required to be separated from the Convertible Notes and accounted for as a freestanding derivative instrument subject to derivative accounting. The allocation of proceeds to the conversion option results in a discount on the Convertible Notes. The Company is amortizing the discount to interest expense over the term of the Convertible Notes using the effective interest method.

The Company presents accrued interest in accrued current liabilities because the notes are currently convertible and the interest is payable in cash. The effective annual interest rate for the Convertible Notes was 19.4%, 14.8%, and 14.8% for the years ended December 31, 2023, 2022, and 2021, respectively.

A summary of the Convertible Notes at December 31, 2023 and 2022 is as follows:

	December 31, 2023	December 31, 2022
Convertible Notes	$ 37,500	$ 37,500
Less: unamortized discount and current portion	(28,362)	(8,751)
Total	$ 9,138	$ 28,749

Interest recognized with regard to the Convertible Notes was as follows:

	Year Ended December 31,		
	2023	2022	2021
Coupon Interest	$ 2,130	2,281	2,281
Amortization of discount	2,042	2,314	2,128
Total	$ 4,172	4,595	4,409

Notes Payable

The Company entered into a credit and security agreement in 2014 (as amended, the "MidCap Credit Agreement") establishing a credit facility (as amended, the "MidCap Credit Facility"). The Company satisfied its obligations under the MidCap Credit Agreement in August 2023, as discussed below. In connection with its satisfaction of its obligations, the Company extinguished the MidCap Credit Facility, and all liens and security interests securing the indebtedness under the MidCap Credit Agreement were released.

In June 2021, the Company entered into a Fourth Amended and Restated Credit and Security Agreement (the "Fourth Amendment") to amend the terms of its debt with existing lenders for total indebtedness of $20,833 and borrowed an incremental $4,167, for a total of $25,000. Under the Fourth Amendment, the Company was required to make interest-only payments through April 2024. Commencing in May 2024, the Company was required to make 19 equal monthly installments of principal in the amount of $1,042, plus interest, then on the maturity date, November 30, 2025 the remaining balance of $5,208 plus the exit fee, as defined below. Amounts borrowed under the MidCap Credit Facility based on the Fourth Amendment were initially at LIBOR base rate, subject to 1.00% floor, plus 6.75%. In addition, a final payment (exit fee) equal to 3.5% of amounts drawn under the MidCap Credit Facility, or $875 based on borrowings of $25,000, was due upon the maturity date of November 30, 2025. The Company had accrued the exit fee through November 30, 2025. The Company accounted for the Fourth Amendment as a modification in accordance with the guidance in ASC 470-50 *Debt*. Amounts paid to the lenders were recorded as debt discount and a new effective interest rate was established.

On March 12, 2023, the Company requested, and received, a protective advance of $2,000 under the MidCap Credit Agreement as a short-term bridge loan in response to the closure of Silicon Valley Bank by the California Department of Financial Protection and Innovation. This protective advance was deemed a credit extension. The Company repaid the full principal amount of $2,000 in March 2023.

On March 31, 2023, the Company entered into Amendment No. 1 to the MidCap Credit Agreement ("Amendment No. 1") to replace the LIBOR-based interest rate provisions of the MidCap Credit Agreement with interest rate provisions based on SOFR, establish a benchmark replacement mechanism and make additional administrative updates. The Company accounted for Amendment No. 1 as a modification in accordance with the guidance in ASC 470-50 *Debt*. Application of the modification accounting guidance did not have a material effect on the carrying amount of the long-term notes payable.

On May 4, 2023, the Company entered into Amendment No. 2 to the MidCap Credit Agreement ("Amendment No. 2"). Amendment No. 2 provided that the Company may maintain up to 50% of its consolidated cash and cash equivalents with banks or financial institutions other than Silicon Valley Bank and made additional administrative updates.

As of December 31, 2022, the Company had a total borrowing capacity of $25,000 under the MidCap Credit Facility, which was fully drawn down. In August 2023, in connection with the Company's establishment of the Barings Credit Facility, the Company paid an aggregate of $26,157 to MidCap Financial Trust and the other lenders party to the MidCap Credit Agreement, comprised of $25,017 in principal and interest accrued thereunder and $1,140 in exit and prepayment fees, in satisfaction of the Company's obligations under the MidCap Credit Agreement. In connection with the payment, all liens and security interests securing the indebtedness under the MidCap Credit Agreement were released. The extinguishment of the MidCap Credit Facility has resulted in a loss of $717, which was charged to gains and losses on extinguishment of debt, net on the consolidated statements of operations and comprehensive loss for the year ended December 31, 2023.

Borrowings outstanding were as follows:

	December 31, 2022
Borrowings outstanding	$ 25,000
Accrued exit fee	335
Unamortized discount	(78)
Long-term notes payable	$ 25,257

10. Derivatives

Barings Credit Agreement

The Barings Credit Agreement (Note 9) contains an embedded Royalty Fee Obligation that meets the criteria to be bifurcated and accounted for separately from the Barings Credit Facility (the "Royalty Fee Derivative Liability"). The Royalty Fee Derivative Liability was recorded at fair value upon the entering into the Barings Credit Facility and is subsequently remeasured to fair value at each reporting period. The Royalty Fee Derivative Liability was initially valued and is remeasured using a "with-and-without" method. The "with-and-without" methodology involves valuing the whole instrument on an as-is basis with the embedded Royalty Fee Obligation and then valuing the instrument without the embedded Royalty Fee Obligation. Royalty payments are estimated using a Monte Carlo simulation. Refer to Note 11 for details regarding the determination of fair value.

A roll-forward of the Royalty Fee Derivative Liability is as follows:

	As of
Balance at August 2, 2023	$ 12,604
Change in fair value	(215)
Balance at December 31, 2023	$ 12,389

Convertible Notes

The Convertible Notes (Note 9) contain the Conversion Option Derivative Liability, an embedded conversion option that meets the criteria to be bifurcated and accounted for separately from the Convertible Notes. The Conversion Option Derivative Liability was recorded at fair value upon the issuance of the Convertible Notes and is subsequently remeasured to fair value at each reporting period. The Conversion Option Derivative Liability was initially valued and are remeasured using a "with-and-without" method. The "with-and-without" methodology involves valuing the whole instrument on an as-is basis with the embedded conversion option and then valuing the instrument without the embedded conversion option. The difference between the entire instrument with the embedded conversion option compared to the instrument without the embedded conversion option is the fair value of the derivative, recorded as the Conversion Option Derivative Liability. Refer to Note 11 for details regarding the determination of fair value.

A roll-forward of the Conversion Option Derivative Liability, including the impact from accounting for the Convertible Notes Amendment, is as follows:

	As of
Balance at December 31, 2021	$ 20,192
Change in fair value	(13,841)
Balance at December 31, 2022	6,351
Change in fair value	4,502
Change in fair value from Convertible Notes Amendment	6,745
Balance at December 31, 2023	$ 17,598

Warrants

In April 2014, the Company entered into a credit facility with Silicon Valley Bank and MidCap Financial SBIC, LP, and it issued the lenders warrants to purchase 100,000 shares of its Series D-1 redeemable convertible preferred stock with an exercise price of $3.00 per share. Upon the closing of the Company's IPO in July 2014, the preferred stock warrants became warrants to purchase an aggregate of 37,878 shares of its common stock with an exercise price of $7.92 per share, with Silicon Valley Bank and MidCap Financial SBIC, LP., each holding warrants of 18,939 shares of common stock.

The Company had warrants for the purchase of 18,939 shares of common stock outstanding with MidCap Financial SBIC, LP at December 31, 2020 at a weighted average exercise price of $7.92 per share and an expiration date of April 17, 2021. On January 29, 2021, holders of warrants to purchase 18,939 shares of common stock at an exercise price of $7.92 exercised their right to purchase their warrants. The exercise price of the warrants was paid through a net share settlement mechanism and as a result the Company issued 11,737 shares of common stock to satisfy the exercise of all the warrants.

There are no warrants outstanding as of December 31, 2023 and 2022, respectively.

11. Risks and Fair Value

Concentration of Credit Risk and of Significant Suppliers and Customers

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and cash equivalents and accounts receivable. The Company has its cash and cash equivalents balances at two accredited financial institutions, in amounts that exceed federally insured limits. The Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

The Company is dependent on a small number of third-party manufacturers to supply products for research and development activities in its preclinical and clinical programs and for sales of its products. The Company's development programs as well as revenue from future product sales could be adversely affected by a significant interruption in the supply of any of the components of these products.

Three specialty distributor customers accounted for the following percentages of the Company's total revenue:

	For the Year Ended December 31, 2023	For the Year Ended December 31, 2022	For the Year Ended December 31, 2021
Customer 1	49 %	44 %	42 %

Customer 2	25	25	26
Customer 3	11	17	17

Three specialty distributor customers accounted for the following percentages of the Company's accounts receivables:

	As of	
	December 31, 2023	December 31, 2022
Customer 1	50 %	52 %
Customer 2	28	24
Customer 3	11	15

Change in Fair Value of Derivative Liabilities

Other income (expenses) from the change in the fair values of derivative liabilities as presented on the Company's consolidated statements of operations and comprehensive loss includes the following:

	For the Year Ended December 31, 2023	For the Year Ended December 31, 2022	For the Year Ended December 31, 2021
Change in the fair value of the Conversion Option Derivative Liability	$ (4,502)	$ 13,841	$ 78,121
Change in the fair value of Royalty Fee Derivative Liability	215	—	—
Barings Royalty Fee	(901)	—	—
	$ (5,188)	$ 13,841	$ 78,121

Fair Value of Financial Assets and Liabilities

The following tables present information about the Company's financial assets and liabilities that are measured at fair value on a recurring basis as of December 31, 2023 and 2022 and indicate the level of the fair value hierarchy utilized to determine such fair value:

	Fair Value Measurements as of December 31, 2023 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ 187,951	$ —	$ —	$ 187,951
Liability:				
Derivative liabilities	$ —	$ —	$ 29,987	$ 29,987

	Fair Value Measurements as of December 31, 2022 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ 30,188	$ —	$ —	$ 30,188
Liability:				
Derivative liability	$ —	$ —	$ 6,351	$ 6,351

During the year ended December 31, 2023 and 2022, there were no transfers between Level 1 and 2.

The carrying value of accounts receivable, prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair value due to the short-term nature of these assets and liabilities. The carrying value of the Company's variable interest rate MidCap Credit Facility was recorded at amortized cost, which approximates fair value due to the variable interest rate.

Barings Credit Agreement and Royalty Fee Derivative Liability

At December 31, 2023, the Barings Credit Facility, net of the Royalty Fee Derivative Liability, was carried at amortized cost totaling $66,590 comprised of the $65,787 non-current liability (Note 9) and $803 accrued interest (Note 8). The estimated fair value of the Barings Credit Facility, without the Royalty Fee Derivative Liability, was $72,295 at December 31, 2023.

The fair value of the Royalty Fee Derivative Liability is estimated using a Monte Carlo simulation. The use of this approach requires the use of Level 3 unobservable inputs. The main inputs when determining the fair value of the Royalty Fee Derivative Liability are the amount and timing of the expected future revenue of the Company, the estimated volatility of these revenues, and the discount rate corresponding to the risk of revenue. The estimated fair value presented is not necessarily indicative of an amount that could be realized in a current market exchange. The use of alternative inputs and estimation methodologies could have a material effect on these estimates of fair value.

The main inputs to valuing the Royalty Fee Derivative Liability are as follows:

	As of December 31, 2023
Revenue volatility	67.0 %
Revenue discount rate	15.8 %

The main inputs to valuing the Royalty Fee Derivative Liability as of the Closing Date were revenue volatility of 61.0%, and a revenue discount rate of 15.8%.

Convertible Notes and Conversion Option Derivative Liability

At December 31, 2023, the Convertible Notes, net of the Conversion Option Derivative Liability, were carried at amortized cost totaling $20,024, comprised of the $9,138 non-current liability (Note 9) and $10,886 accrued interest (Note 8). At December 31, 2022, the Convertible Notes, net of the Conversion Option Derivative Liability, were carried at amortized cost totaling $37,505, comprised of the $28,749 non-current liability (Note 9) and $8,756 accrued interest (Note 8). The estimated fair value of the Convertible Notes, without the Conversion Option Derivative Liability, was $22,665 and $33,177 at December 31, 2023 and 2022, respectively.

The fair value of the Convertible Notes with and without the conversion option is estimated using a binomial lattice approach. The use of this approach requires the use of Level 3 unobservable inputs. The main input when determining the fair value of the Convertible Notes is the bond yield that pertains to the host instrument without the conversion option. The significant assumption used in determining the bond yield is the market yield movements of a comparable instrument issued as of the valuation date, which is assessed and updated each period. The main input when determining the fair value for disclosure purposes is the bond yield which is updated each period to reflect the yield of a comparable instrument issued as of the valuation date. The estimated fair value presented is not necessarily indicative of an amount that could be realized in a current market exchange. The use of alternative inputs and estimation methodologies could have a material effect on these estimates of fair value.

The main inputs to valuing the Convertible Notes with the conversion option are as follows:

	As of	
	December 31, 2023	December 31, 2022
Company's stock price	$ 4.46	$ 2.81
Volatility	88.4 %	93.8 %

Bond yield	20.8 %	16.2 %

The bond yield was derived by making the fair value of the Convertible Notes equal to the face value on the issuance date. Fair value measurements are highly sensitive to changes in these inputs and significant changes in these inputs would result in a significantly higher or lower fair value.

12. Equity

Preferred Stock

The Amended and Restated Certificate of Incorporation authorized 5,000,000 shares of preferred stock, $0.0001 par value, all of which is undesignated and none of which are issued or outstanding at December 31, 2023 and 2022.

Common Stock

The Amended and Restated Certificate of Incorporation authorized 100,000,000 shares of the Company's common stock. Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. In June 2021, the Company adopted an amended and restated certificate of incorporation increasing the number of its authorized shares of its common stock to 200,000,000 shares.

On April 5, 2019, the Company entered into an Open Market Sales Agreement (the "2019 Sales Agreement") with Jefferies LLC ("Jefferies"), under which the Company may offer and sell its common stock having aggregate proceeds of up to $50,000 from time-to-time through Jefferies, acting as agent. The Company did not sell any shares of common stock under the 2019 Sales Agreement in the twelve months ended December 31, 2021. On August 9, 2021, the Company and Jefferies mutually terminated the 2019 Sales Agreement and entered into another Open Market Sale Agreement (the "2021 Sales Agreement") under which the Company may offer and sell shares of common stock of the Company having an aggregate offering price of up to $100,000 from time to time through Jefferies, acting as agent. In the twelve months ended December 31, 2023, the Company sold 1,514,926 shares of common stock under the 2021 Sales Agreement, resulting in gross proceeds to the Company of $9,897, and net proceeds, after accounting for issuance costs, of $9,532. The Company did not offer or sell shares of its common stock under the 2021 Sales Agreement during the twelve months ended December 31, 2022 and 2021, respectively.

On December 13, 2023, the Company entered into an underwriting agreement with Jefferies, BofA Securities, Inc. and Piper Sandler & Co. (collectively "the Underwriters") in connection with an underwritten public offering of 30,800,000 shares of the Company's common stock. Under the terms of this underwriting agreement, the Company also granted the Underwriters an option to purchase up to an additional 4,620,000 shares of common stock at the public offering price, less the underwriting discounts and commissions. On December 17, 2023, the Company sold all 35,420,000 shares of common stock and closed this underwritten public offering. The public offering price of the shares in this offering was $3.25 per share, and the Underwriters purchased all of the shares from the Company at a price of $3.055 per share. After deducting underwriting discounts and commissions and offering expenses, the Company received net proceeds from the offering of $107,725.

As of December 31, 2023, the Company had reserved 24,933,970 shares of common stock for the exercise of outstanding stock options, the vesting of restricted stock units, and the number of shares remaining available for grant under its stock-based compensation plans (Note 13).

13. Stock-Based Awards

For the years ended December 31, 2023 and 2022, the Company had four stock-based compensation plans under which it was able to grant stock-based awards, the 2014 Stock Incentive Plan (the "2014 Plan"), the 2021 Stock Incentive Plan (the "2021 Plan"), the 2019 Inducement Stock Incentive Plan (the "2019 Inducement Plan"), and the 2014 Employee Stock Purchase Plan (the "ESPP") (collectively the "Stock Plans"). Certain inducement awards made prior to inception of the 2019 Inducement Plan were issued outside of the Stock Plans. The purpose of the Stock Plans is to provide incentives to employees, directors, and nonemployee consultants. The 2014 Plan and the 2021 Plan provide for the grant of incentive stock options, non-statutory stock options, restricted stock awards, restricted stock units ("RSUs"), stock appreciation rights and other stock-based awards. As of December 31, 2023 and 2022, respectively, the Company had an immaterial number of vested stock awards outstanding that were granted under the Company's 2006 Stock Incentive Plan (the "2006 Plan"). Effective as of the adoption of the 2014 Plan by the Company's stockholders in 2014, no new awards have been granted under the 2006 Plan. As of December 31, 2023, all then outstanding awards under the 2006 Plan remained in effect and continued to be governed by the terms of the 2006 Plan.

2014 Plan - The number of shares initially reserved for issuance under the 2014 Plan was 1,336,907 shares of common stock. Between 2014 and 2021, the number of shares reserved for issuance under the 2014 Plan increased to 8,622,647 as of January 1, 2021. On June 18, 2021, the Company's stockholders approved the adoption of the 2021 Plan previously approved by the board of directors. Effective as of the adoption of the 2021 Plan by the Company's stockholders, no new awards have been granted under the 2014 Plan. However, as of December 31, 2023, all then-outstanding awards under the 2014 Plan remained in effect and continued to be governed by the terms of the 2014 Plan.

2021 Plan - The number of shares initially reserved for issuance under the 2021 Plan was 6,000,000 shares of common stock; plus 456,334 shares remaining available for grant under the 2014 Plan as of immediately prior to the effective date of the 2021 Plan and 9,766,336 shares subject to awards granted under the 2014 Plan or the 2006 Plan, which awards expire, terminate or are otherwise surrendered, canceled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right (subject to certain limitations). On June 16, 2022, the Company's stockholders approved an amendment ("Amendment No. 1") to the Company's 2021 Plan. Amendment No. 1 increased the number of shares of common stock that is reserved for issuance under the 2021 Plan by 3,600,000. On June 14, 2023, the Company's stockholders approved an amendment ("Amendment No. 2") to the Company's 2021 Plan. Amendment No. 2 increased the number of shares of common stock that is reserved for issuance under the 2021 Plan by 3,900,000. As of December 31, 2023, 6,219,678 shares remained available for issuance under the 2021 Plan.

2019 Inducement Plan - The 2019 Inducement Plan provides for the following types of awards, each of which is referred to as an "Award": non-statutory stock options, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards. Awards under the 2019 Inducement Plan may only be granted to persons who (a) were not previously an employee or director of the Company or (b) are commencing employment with the Company following a bona fide period of non-employment, in either case as an inducement material to the individual's entering into employment with the Company and in accordance with the requirements of Nasdaq Stock Market Rule 5635(c)(4). For the avoidance of doubt, neither consultants nor advisors shall be eligible to participate in the 2019 Inducement Plan. Each person who is granted an Award under the 2019 Inducement Plan is deemed a "Participant". On December 10, 2020, the board of directors of the Company amended the 2019 Inducement Plan to increase the aggregate number of shares issuable by 554,000 shares of common stock to 1,054,000. As of December 31, 2023, 551,375 shares remained available for issuance under the 2019 Inducement Plan.

ESPP – The number of shares initially reserved for issuance under the ESPP was 207,402 shares of common stock. The number of shares of common stock that may be issued under the ESPP will automatically increase on the first day of each fiscal year, commencing on January 1, 2015 and ending on December 31, 2024, in an amount equal to the least of 207,402 shares of the Company's common stock, 0.5% of the number of shares of the Company's common stock outstanding on the first day of the applicable fiscal year, and an amount determined by the Company's board of directors. On January 1, 2023, the number of shares available for issuance under the ESPP increased by 207,402. As of December 31, 2023, 398,784 shares of common stock remained available for issuance.

Stock options granted pursuant to the Stock Plans, excluding awards under the ESPP, are granted at exercise prices not to be less than the fair value of common shares as of the date of grant. They generally require a service period of 4 years and generally vest monthly, or 1/4 on the first anniversary of the grant date, with the remainder vesting monthly over the remaining three years. Stock Options granted under the 2019 Inducement Plan may in addition be subject to performance-based vesting. The maximum contractual term of Stock Options granted under the Stock Plans is generally 10 years. RSUs granted pursuant to the Stock Plans generally require a service period of 3 years and generally vest 1/3 on each anniversary of the grant date.

Valuation of Awards

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model. The expected life of the options was calculated using the simplified method. The simplified method defines the life as the average of the contractual term of the options and the weighted-average vesting period for all option tranches. The Company utilizes the simplified method because the Company does not have sufficient historical exercise data over the life of awards to provide a reasonable basis upon which to estimate expected term. The expected term of stock options granted to nonemployees is equal to the contractual term of the option award. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future. The Company uses its historical volatility to estimate expected volatility.

The assumptions that the Company used to determine the fair value of the stock options granted to employees and directors are as follows, presented on a weighted average basis:

	Year Ended December 31,		
	2023	2022	2021
Risk-free interest rate	3.72 %	2.10 %	0.80 %
Expected term (in years)	6	6	6
Expected volatility	77.32 %	81.14 %	87.65 %
Expected dividend yield	— %	— %	— %

For RSUs, the grant date fair value is the closing price of the Company's stock on the grant date.

Stock Options

The following table summarizes the Company's stock option activity:

	Shares Issuable Under Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (In years)	Aggregate Intrinsic Value
Outstanding as of December 31, 2022	13,669,711	$ 8.45	7.0	$ 7
Granted	3,542,491	4.00		
Exercised	(141,952)	3.88		
Cancelled/forfeited	(933,459)	8.63		
Outstanding as of December 31, 2023	16,136,791	$ 7.51	6.1	$ 3,364
Options vested and expected to vest as of December 31, 2023	14,859,010	$ 7.48	5.9	$ 2,910
Options exercisable as of December 31, 2023	11,073,110	$ 8.18	5.0	$ 1,648

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those stock options that had exercise prices lower than the fair value of the Company's common stock. The aggregate intrinsic value of stock options exercised was $275, $186 and $6,779 during the years ended December 31, 2023, 2022 and 2021, respectively.

The weighted average grant date fair value of stock options granted to employees and directors during the years ended December 31, 2023, 2022 and 2021 was $2.74, $4.95 and $12.48 per share, respectively.

As of December 31, 2023, there were 67,509 outstanding unvested service-based stock options held by nonemployees.

RSUs

The following table summarizes the Company's activity of unvested RSUs:

	RSU's	Weighted average grant date fair value
Unvested balance at December 31, 2022	1,092,682	$ 5.03
Granted	1,113,964	4.00
Released	(393,805)	4.89
Cancelled/forfeited	(185,500)	4.75
Unvested balance at December 31, 2023	1,627,341	$ 4.40

Each RSU is equivalent to one share of common stock upon vesting. Typically, each RSU award vests on an annual basis over a three-year period. Holders of RSUs are not entitled to vote on any matters and are not entitled to dividends. The Company has determined the fair value of each RSU based on the closing price of the Company's common stock on the date of grant and recognizes the compensation expense using the straight-line method over the service period, which coincides with the vesting period.

Stock-based Compensation

The Company recorded stock-based compensation expense in the following expense categories of its statements of operations and comprehensive loss:

	Year Ended December 31,		
	2023	2022	2021
Research and development	$ 4,508	$ 4,166	$ 3,750
Selling and marketing	3,682	4,684	4,014
General and administrative	9,635	8,114	7,214
	$ 17,825	$ 16,964	$ 14,978

As of December 31, 2023, the Company had an aggregate of $16,537 of unrecognized stock-based compensation cost, which is expected to be recognized over a weighted average period of 2.02 years.

14. Employee Benefits

The Company established a defined contribution savings plan under Section 401(k) of the Internal Revenue Code (the "401(k) Plan"). The 401(k) Plan covers substantially all employees who meet minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. Company contributions to the plan may be made at the discretion of the board of directors. For the years ended December 31, 2023, 2022 and 2021, the Company has made contributions of $625, $593, and $493, respectively, to the 401(k) Plan.

15. Income Taxes

During the years ended December 31, 2023, 2022 and 2021, the Company recorded no income tax benefits for the net operating losses incurred or the research and development tax credits generated in each year, due to its uncertainty of realizing a benefit from those items.

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,		
	2023	2022	2021
Federal statutory income tax rate	21.0 %	21.0 %	21.0 %
Research and development tax credits	3.6	5.4	35.9
State taxes, net of federal benefit	2.0	2.6	19.3
Stock-based compensation	(2.3)	(2.1)	(7.8)
Derivative liability	—	2.7	244.7
Change in tax rate	(0.4)	1.4	(8.4)
Other	(0.2)	(0.1)	(3.8)
Change in the valuation allowance	(23.7)	(30.9)	(300.9)
Effective income tax rate	— %	— %	— %

Changes in the valuation of the Royalty Fee Derivative Liability, except to the extent that they relate to actual royalties paid or accrued, do not provide a future tax benefit. To the extent the deferred tax asset related to the Royalty Fee Derivative Liability exceeds the deferred tax liability related to the Barings Credit Agreement, the excess is recorded as a permanent item. Changes in the valuation of the Conversion Option Derivative Liability do not provide a future tax benefit. To the extent the deferred tax asset related to the Conversion Option Derivative Liability exceeds the deferred tax liability related to the Convertible Notes, the excess is recorded as a permanent item.

Net deferred tax assets consisted of the following:

	December 31,	
	2023	2022
Deferred tax assets:		
Net operating loss carryforwards	$ 120,971	$ 113,801
Tax credit carryforwards	22,597	19,653
Capitalized start-up costs	121	255
Capitalized research and development expenses, net - Sec. 59(e)	3,570	5,773
Capitalized research and development expenses, net Sec. 174	19,491	10,046
Operating lease liabilities	1,970	2,422
Derivative liability	6,981	1,497
Stock-based Awards	10,443	8,783
Accrued expenses and other	8,433	6,274
Total deferred tax assets	194,577	168,504
Valuation allowance	(183,737)	(164,546)
Net deferred tax assets	10,840	3,958
Deferred tax liabilities:		
Operating lease right of use assets	(1,507)	(1,895)
Convertible Notes	(6,603)	(2,063)
Barings Credit Facility	(2,730)	—
Total deferred tax liabilities	(10,840)	(3,958)
Net deferred tax assets	$ —	$ —

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2023, 2022 and 2021 related primarily to the increase in net operating loss carryforwards, amortization of capitalized research and development expenses, and increase in research and development tax credit carryforwards were as follows:

	Year Ended December 31,		
	2023	2022	2021
Valuation allowance as of beginning of year	$ 164,546	$ 142,637	$ 123,020
Increases recorded to income tax provision	19,191	21,909	19,617
Valuation allowance as of end of year	$ 183,737	$ 164,546	$ 142,637

As of December 31, 2023, the Company had net operating loss ("NOL") carryforwards for federal and state income tax purposes of $482,561 and $343,803, respectively. The federal and state NOLs generated for annual periods prior to January 1, 2018 begin to expire in 2026. The Company's federal NOLs generated for the years ended since December 31, 2018, which amounted to a total of $356,757, can be carried forward indefinitely. As of December 31, 2023, the Company also had available research and development tax credit carryforwards for federal and state income tax purposes of $15,383 and $8,794, respectively, which begin to expire in 2026 and 2025, respectively. Utilization of the NOL carryforwards and research and development tax credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986 ("Section 382") due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain shareholders or public groups in the stock of a corporation by more than 50% over a three-year period. The Company has not conducted a study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception due to the significant complexity and cost associated with such a study. If the Company has experienced a change of control, as defined by Section 382, at any time since inception, utilization of the NOL carryforwards or research and development tax credit carryforwards would be subject to an annual limitation under Section 382, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments, as required. Any limitation may result in expiration of a portion of the NOL carryforwards or research and development tax credit carryforwards before utilization. Further, until a study is completed and any limitation is known, no amounts are being presented as an uncertain tax position.

The Company has evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets. Management considered the Company's cumulative net losses and concluded that it is more likely than not that the Company would not realize the benefits of the deferred tax assets. Accordingly, a full valuation allowance was established against the net deferred tax assets as of December 31, 2023, 2022 and 2021.

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2023, 2022 or 2021.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. There are currently no pending income tax examinations. The Company's tax years are still open under statute from the Company's fiscal year 2019 to the present. Earlier years may be examined to the extent that tax credit or net operating loss carryforwards are used in future periods.

16. Net Loss Per Share

Basic and diluted net loss per share attributable to common stockholders was calculated as follows for the years ended December 31, 2023, 2022 and 2021:

	Year ended December 31,		
	2023	2022	2021
Numerator:			
Net loss attributable to common stockholders	$ (80,736)	$ (71,038)	$ (6,553)
Denominator:			
Weighted average common shares outstanding, basic	79,827,362	76,875,035	76,392,870
Net loss per share - basic	$ (1.01)	$ (0.92)	$ (0.09)

Basic and diluted net loss per share was calculated as follows for the years ended December 31, 2023, 2022 and 2021:

	Year Ended December 31,		
	2023	2022	2021
Net loss attributable to common stockholders, basic	$ (80,736)	$ (71,038)	$ (6,553)
Interest expense on Convertible Notes	4,172	4,596	4,409
Gain on extinguishment of debt (Note 9)	(14,907)	—	—
Change in fair value of derivative liability	4,502	(13,841)	(78,121)
Net loss attributable to common stockholders, diluted	$ (86,969)	$ (80,283)	$ (80,265)
Weighted average common shares outstanding, basic	79,827,362	76,875,035	76,392,870
Dilutive options (treasury stock method)	—	—	—
Shares issuable upon conversion of Convertible Notes, as if converted	5,769,232	5,769,232	5,769,232
Weighted average common shares outstanding, diluted	85,596,594	82,644,267	82,162,102
Net loss per share attributable to common stockholders, diluted	$ (1.02)	$ (0.97)	$ (0.98)

The Company excluded the following common stock equivalents, outstanding as of December 31, 2023, 2022 and 2021 from the computation of diluted net loss per share attributable to common stockholders for the years ended December 31, 2023, 2022 and 2021 because they had an anti-dilutive impact due to the net loss incurred for the periods.

	December 31,		
	2023	2022	2021
Options to purchase common stock	16,136,791	13,669,711	10,934,828
Restricted stock units	1,627,341	1,092,682	—
	17,764,132	14,762,393	10,934,828

17. Commitments and Contingencies

Indemnification Agreements

In the ordinary course of business, the Company enters into agreements that may include indemnification provisions. Pursuant to such agreements, the Company may indemnify, hold harmless and defend indemnified parties for losses suffered or incurred by the indemnified party. Some of the provisions will limit losses to those arising from third-party actions. In some cases, the indemnification will continue after the termination of the agreement. The maximum potential amount of future payments the Company could be required to make under these provisions is not determinable. To date, the Company has not incurred any material costs as a result of such indemnifications.

18. Related Party Transactions

The Company has engaged Wilmer Cutler Pickering Hale and Dorr LLP (“WilmerHale”) to provide certain legal services to the Company. The sister of the Company's former Chief Business Officer Christopher White was a managing partner at WilmerHale, who has not participated in providing legal services to the Company. The Company incurred fees for legal services rendered by WilmerHale of approximately $1,472, $959 and $1,396 for the years ended December 31, 2023, 2022 and 2021, respectively. As of December 31, 2023 and 2022, there was $298 and $0 recorded in accounts payable for WilmerHale. As of December 31, 2023 and 2022, there was $0 and $24 recorded in accrued expenses for WilmerHale.

The Company has engaged Heier Consulting, LLC (“Heier Consulting”), an entity affiliated with Jeffrey Heier, M.D. a former member of the Company’s Board of Directors and the Company’s current Chief Scientific Officer, to provide advice or expertise on one or more of the Company’s development-stage drug or medical device products relating to retinal diseases or conditions under a consultant agreement. Compensation for these services is in the form of cash and stock-based awards. The total grant date fair value of stock-based awards granted to Heier Consulting is $96, which is recognized to expense on a straight-line basis over the respective vesting periods. The Company incurred cash-based fees for services rendered by Heier Consulting of approximately $32, 24, and $0 for the years ended December 31, 2023, 2022 and 2021, respectively. As of December 31, 2023 and 2022, there was $6 and $3 recorded in accounts payable for Heier Consulting. As of December 31, 2023 and 2022, there was $0 and $0 recorded in accrued expenses for Heier Consulting. Effective February 21, 2024, the Company and Heier Consulting terminated this relationship.

In November 2020, the Company engaged Specialty Pharma Consulting, LLC ("Specialty Pharma"), an entity affiliated with Kevin Coughenour, to provide services for quality engineering and validation activities in the ordinary course of business. Mr. Coughenour is married to the Company's former Chief Operating Officer Patricia Kitchen. On April 26, 2021, the Company and Specialty Pharma terminated their relationship. The Company incurred fees for quality engineering and validation activities rendered by Specialty Pharma of $0, $0 and $155 for the years ended December 31, 2023, 2022 and 2021, respectively. As of December 31, 2023 and 2022, there were no liabilities recorded with regard to Specialty Pharma.

19. Subsequent Events

Securities Purchase Agreement

On February 21, 2024, the Company, entered into a securities purchase agreement (the "Securities Purchase Agreement") with certain institutional accredited investors (the "Investors"), pursuant to which the Company issued and sold to the Investors in a private placement an aggregate of 32,413,560 shares of the Company's common stock, par value $0.0001 per share (the "Shares"), at a price of $7.52 per share, and, to certain Investors in lieu of Shares, pre-funded warrants to purchase 10,805,957 shares of the Company's common stock (the "Pre-Funded Warrants"), at a price of $7.519 per Pre-Funded Warrant (the "2024 Private Placement"). Each Pre-Funded Warrant issued in the 2024 Private Placement has an exercise price of $0.001 per share, is currently exercisable and will remain exercisable until the Pre-Funded Warrant is exercised in full. The 2024 Private Placement closed on February 26, 2024. The Company received aggregate gross proceeds from the 2024 Private Placement of approximately $325,000, before deducting placement agent fees and offering expenses.

2019 Inducement Plan

On February 20, 2024, the Company's board of directors amended the 2019 Inducement Plan to increase the aggregate number of shares issuable thereunder from 1,054,000 to 3,804,000 shares of common stock. On February 22, 2024, the Company granted a total of 1,527,019 non-statutory stock options and a total of 935,279 RSUs under the 2019 Inducement Plan to the Company's newly appointed Executive Chairman and its new Chief Strategy Officer.

ESPP

The number of shares of common stock that may be issued under the ESPP will automatically increase on the first day of each fiscal year, commencing on January 1, 2015 and ending on December 31, 2024, in an amount equal to the least of 207,402 shares of the Company's common stock, 0.5% of the number of shares of the Company's common stock outstanding on the first day of the applicable fiscal year, and an amount determined by the Company's board of directors. On January 1, 2024, the number of shares available for issuance under the ESPP increased by 207,402.

OCULAR THERAPEUTIX, INC.

RESTRICTED STOCK UNIT AGREEMENT

Ocular Therapeutix, Inc. (the "Company") hereby grants the following restricted stock units pursuant to its 2019 Inducement Stock Incentive Plan. The terms and conditions attached hereto are also a part hereof.

Notice of Grant

Name of recipient (the "Participant"):	
Grant Date:	
Number of restricted stock units ("RSUs") granted:	
Number, if any, of RSUs that vest immediately on the grant date:	
RSUs that are subject to vesting schedule:	
Vesting Start Date:	

Vesting Schedule:

Vesting Date:	Number of RSUs that Vest:
All vesting is dependent on the Participant remaining an Eligible Participant, as provided herein.	

This grant of RSUs satisfies in full all commitments that the Company has to the Participant with respect to the issuance of stock, stock options or other equity securities.

Ocular Therapeutix, Inc.

____
Signature of Participant

____
Street Address

____
City/State/Zip Code

By:___________________________
Name of Officer
Title:

Ocular Therapeutix, Inc.

Restricted Stock Unit Agreement
Incorporated Terms and Conditions

1. Award of Restricted Stock Units. In consideration of services rendered and to be rendered to the Company, by the Participant, an employee of the Company, the Company has granted to the Participant, subject to the terms and conditions set forth in this Restricted Stock Unit Agreement (this "Agreement") and in the Company's 2019 Inducement Stock Incentive Plan (the "Plan"), an award with respect to the number of restricted stock units (the "RSUs") set forth in the Notice of Grant that forms part of this Agreement (the "Notice of Grant"). Each RSU represents the right to receive one share of common stock, $0.0001 par value per share, of the Company (the "Common Stock") upon vesting of the RSU, subject to the terms and conditions set forth herein.

The RSUs evidenced by this agreement were granted to the Participant pursuant to the inducement grant exception under Nasdaq Stock Market Rule 5635(c)(4), as an inducement that is material to the Participant's employment with the Company.

2. Vesting. The RSUs shall vest in accordance with the Vesting Schedule set forth in the Notice of Grant (the "Vesting Schedule"). Any fractional shares resulting from the application of any percentages used in the Vesting Schedule shall be rounded down to the nearest whole number of RSUs. As soon as practicable after the vesting of the RSU, the Company will deliver to the Participant, for each RSU that becomes vested, one share of Common Stock, subject to the payment of any taxes pursuant to Section 7. The Common Stock will be delivered to the Participant as soon as practicable following each vesting date, but in any event within 30 days of such date.

3. Forfeiture of Unvested RSUs Upon Cessation of Service. In the event that the Participant ceases to be an Eligible Participant (as defined below) for any reason or no reason, with or without cause, all of the RSUs that are unvested as of the time of such cessation shall be forfeited immediately and automatically to the Company, without the payment of any consideration to the Participant, effective as of such cessation. The Participant shall have no further rights with respect to the unvested RSUs or any Common Stock that may have been issuable with respect thereto. The Participant shall be an "Eligible Participant" if the individual is an employee, director or officer of, or consultant or advisor to, the Company or any other entity the employees, officers, directors, consultants or advisors of which are eligible to receive awards of RSUs under the Plan.

4. Restrictions on Transfer. The Participant shall not sell, assign, transfer, pledge, hypothecate, encumber or otherwise dispose of, by operation of law or otherwise (collectively "transfer") any RSUs, or any interest therein. The Company shall not be required to treat as the owner of any RSUs or issue any Common Stock to any transferee to whom such RSUs have been transferred in violation of any of the provisions of this Agreement.

5. Rights as a Stockholder. The Participant shall have no rights as a stockholder of the Company with respect to any shares of Common Stock that may be issuable with respect to

the RSUs until the issuance of the shares of Common Stock to the Participant following the vesting of the RSUs.

6. Provisions of the Plan. This Agreement is subject to the provisions of the Plan, a copy of which is furnished to the Participant with this Agreement.

7. Tax Matters.

(a) Acknowledgments; No Section 83(b) Election. The Participant acknowledges that he or she is responsible for obtaining the advice of the Participant's own tax advisors with respect to the award of RSUs and the Participant is relying solely on such advisors and not on any statements or representations of the Company or any of its agents with respect to the tax consequences relating to the RSUs. The Participant understands that the Participant (and not the Company) shall be responsible for the Participant's tax liability that may arise in connection with the acquisition, vesting and/or disposition of the RSUs. The Participant acknowledges that no election under Section 83(b) of the Internal Revenue Code of 1986, as amended, (the "Code") is available with respect to RSUs.

(b) Withholding. The Participant acknowledges and agrees that the Company has the right to deduct from payments of any kind otherwise due to the Participant any federal, state, local or other taxes of any kind required by law to be withheld with respect to the vesting of the RSUs. To the extent the Participant has not previously executed and delivered to the Company effective durable sell-to-cover instructions that by their terms would cover any taxes required by law to be withheld with respect to the vesting of the RSUs, at such time as the Participant is not aware of any material nonpublic information about the Company or the Common Stock and the Participant is not subject to any restriction on trading activities with respect to the Common Stock pursuant to any Company insider trading or other policy, the Participant shall execute the instructions set forth in Schedule A attached hereto (the "Durable Automatic Sell-to-Cover Instructions") as the means of satisfying such tax obligation, unless the Participant has already executed such Durable Automatic Sell-to-Cover Instructions and the Company has such instructions on file. If the Participant has not executed the Durable Automatic Sell-to-Cover Instructions prior to an applicable vesting date, then the Participant agrees that if under applicable law the Participant will owe taxes at such vesting date on the portion of the award then vested the Company shall be entitled to immediate payment from the Participant of the amount of any tax required to be withheld by the Company. The Company shall not deliver any shares of Common Stock to the Participant until it is satisfied that all required withholdings have been made.

8. Miscellaneous.

(a) Section 409A. The RSUs awarded pursuant to this Agreement are intended to be exempt from or comply with the requirements of Section 409A of the Code and the Treasury Regulations issued thereunder ("Section 409A"). The delivery of shares of Common Stock on the vesting of the RSUs may not be accelerated or deferred unless permitted or required by Section 409A.

(b) Participant's Acknowledgements. The Participant acknowledges that he or she: (i) has read this Agreement; (ii) has been represented in the preparation, negotiation and execution of this Agreement by legal counsel of the Participant's own choice or has voluntarily declined to seek such counsel; (iii) understands the terms and consequences of this Agreement; (iv) is fully aware of the legal and binding effect of this Agreement; and (v) agrees that in accepting this award, the Participant will be bound by any clawback policy that the Company has adopted or may adopt in the future.

Schedule A

DURABLE AUTOMATIC SELL-TO-COVER INSTRUCTIONS

This Durable Automatic Sell-to-Cover Instruction (this "Instruction"), which is being delivered to Ocular Therapeutix, Inc. (the "Company") by the undersigned on the date set forth below (the "Adoption Date"), relates to the Covered RSUs (as defined following my signature below). This Instruction provides for "eligible sell-to-cover transactions" (as described in Rule 10b5-1(c)(1)(ii)(D)(3) under the Securities Exchange Act of 1934 (the "Exchange Act")) and is intended to satisfy the affirmative defense conditions of Rule 10b5-1(c)(1) under the Exchange Act.

I acknowledge that upon vesting and settlement of any Covered RSUs in accordance with the applicable RSU's terms, whether vesting is based on the passage of time or the achievement of performance goals, I will have compensation income equal to the fair market value of the shares of the Company's Common Stock subject to the RSUs that are settled on such settlement date and that the Company is required to withhold income and employment taxes in respect of that compensation income.

I desire to establish a plan and process to satisfy such withholding obligation in respect of all Covered RSUs through an automatic sale of a portion of the shares of the Company's Common Stock that would otherwise be issuable to me on each applicable settlement date, such portion to be in an amount sufficient to satisfy such withholding obligation, with the proceeds of such sale delivered to the Company in satisfaction of such withholding obligation.

I understand that the Company has arranged for the administration and execution of its equity incentive plans and the sale of securities by plan participants thereunder pursuant to a platform administered by a third party (the "Administrator") and the Administrator's designated brokerage partner.

Upon the settlement of any of my Covered RSUs pursuant to the Agreement after the [30th day following the Adoption Date][1] [later of: (i) the 90th day following the Adoption Date or (ii) two business days following the disclosure of the Company's financial results in Form 10-Q or Form 10-K for the completed fiscal quarter in which the Adoption Date occurs (or, with respect to this clause (ii), if sooner, the 120th day after the Adoption Date)][2], I hereby appoint the Administrator (or any successor administrator) to automatically sell such number of shares of the Company's Common Stock issuable with respect to such RSUs that vested and settled as is sufficient to generate net proceeds sufficient to satisfy the Company's minimum statutory

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1 For a Participant who is not a Section 16 officer of the Company, insert "30th day following the Adoption Date".

2 For a Participant who is a Section 16 officer of the Company, insert "later of: (i) the 90th day following the Adoption Date or (ii) two business days following the disclosure of the Company's financial results in Form 10-Q or Form 10-K for the completed fiscal quarter in which this Instruction was adopted (or, with respect to this clause (ii), if sooner, the 120th day after adoption of this Instruction)" or, alternatively, "120th day following the Adoption Date".

withholding obligations with respect to the income recognized by me in connection with the vesting and settlement of such RSUs (based on minimum statutory withholding rates for all tax purposes, including payroll and social security taxes, that are applicable to such income), and the Company shall receive such net proceeds in satisfaction of such tax withholding obligation.

I hereby appoint the Chief Executive Officer, the Chief Financial Officer and the Corporate Counsel, and any of them acting alone and with full power of substitution, to serve as my attorneys-in-fact to arrange for the sale of shares of the Company's Common Stock in accordance with this Instruction. I agree to execute and deliver such documents, instruments and certificates as may reasonably be required in connection with the sale of the shares of Common Stock pursuant to this Instruction.

I hereby certify that, as of the Adoption Date:

(i) I am not prohibited from entering into this Instruction by the Company's insider trading policy or otherwise;

(ii) I am not aware of any material nonpublic information about the Company or its Common Stock; and

(iii) I am adopting this Instruction in good faith and not as part of a plan or scheme to evade the prohibitions of Rule 10b-5 under the Exchange Act.

____

Print Name: ______________________

Date: ___________________________

Covered RSUs:

The first award of RSUs granted to me on or after ______________ [*insert date of grant of current RSUs the grant of which is triggering the execution of this Instruction; if instruction is being executed in advance of a grant of RSUs, insert the Adoption Date*] and any RSUs that may, from time to time following such date, be granted to me by the Company, other than any future granted RSUs which by the terms of the applicable award agreement require the Company to withhold shares for tax withholding obligations in connection with the vesting and settlement of such RSUs, and therefore do not permit sell-to-cover transactions, are covered by this Instruction.

OCULAR THERAPEUTIX, INC.

RESTRICTED STOCK UNIT AGREEMENT

Ocular Therapeutix, Inc. (the "Company") hereby grants the following restricted stock units pursuant to its 2021 Stock Incentive Plan, as amended. The terms and conditions attached hereto are also a part hereof.

Notice of Grant

Name of recipient (the "Participant"):	
Grant Date:	
Number of restricted stock units ("RSUs") granted:	
Number, if any, of RSUs that vest immediately on the grant date:	
RSUs that are subject to vesting schedule:	
Vesting Start Date:	

Vesting Schedule:

Vesting Date:	Number of RSUs that Vest:
All vesting is dependent on the Participant remaining an Eligible Participant, as provided herein.	

This grant of RSUs satisfies in full all commitments that the Company has to the Participant with respect to the issuance of stock, stock options or other equity securities.

Ocular Therapeutix, Inc.

____
Signature of Participant

____
Street Address

____
City/State/Zip Code

By:__________________________
Name of Officer
Title:

Ocular Therapeutix, Inc.

Restricted Stock Unit Agreement
Incorporated Terms and Conditions

1. Award of Restricted Stock Units. In consideration of services rendered and to be rendered to the Company, by the Participant, the Company has granted to the Participant, subject to the terms and conditions set forth in this Restricted Stock Unit Agreement (this "Agreement") and in the Company's 2021 Stock Incentive Plan, as amended (the "Plan"), an award with respect to the number of restricted stock units (the "RSUs") set forth in the Notice of Grant that forms part of this Agreement (the "Notice of Grant"). Each RSU represents the right to receive one share of common stock, $0.0001 par value per share, of the Company (the "Common Stock") upon vesting of the RSU, subject to the terms and conditions set forth herein.

2. Vesting. The RSUs shall vest in accordance with the Vesting Schedule set forth in the Notice of Grant (the "Vesting Schedule"). Any fractional shares resulting from the application of any percentages used in the Vesting Schedule shall be rounded down to the nearest whole number of RSUs. As soon as practicable after the vesting of the RSU, the Company will deliver to the Participant, for each RSU that becomes vested, one share of Common Stock, subject to the payment of any taxes pursuant to Section 7. The Common Stock will be delivered to the Participant as soon as practicable following each vesting date, but in any event within 30 days of such date.

3. Forfeiture of Unvested RSUs Upon Cessation of Service. In the event that the Participant ceases to be an Eligible Participant (as defined below) for any reason or no reason, with or without cause, all of the RSUs that are unvested as of the time of such cessation shall be forfeited immediately and automatically to the Company, without the payment of any consideration to the Participant, effective as of such cessation. The Participant shall have no further rights with respect to the unvested RSUs or any Common Stock that may have been issuable with respect thereto. The Participant shall be an "Eligible Participant" if the individual is an employee, director or officer of, or consultant or advisor to, the Company or any other entity the employees, officers, directors, consultants or advisors of which are eligible to receive awards of RSUs under the Plan.

4. Restrictions on Transfer. The Participant shall not sell, assign, transfer, pledge, hypothecate, encumber or otherwise dispose of, by operation of law or otherwise (collectively "transfer") any RSUs, or any interest therein. The Company shall not be required to treat as the owner of any RSUs or issue any Common Stock to any transferee to whom such RSUs have been transferred in violation of any of the provisions of this Agreement.

5. Rights as a Stockholder. The Participant shall have no rights as a stockholder of the Company with respect to any shares of Common Stock that may be issuable with respect to the RSUs until the issuance of the shares of Common Stock to the Participant following the vesting of the RSUs.

6. Provisions of the Plan. This Agreement is subject to the provisions of the Plan, a copy of which is furnished to the Participant with this Agreement.

7. Tax Matters.

(a) Acknowledgments; No Section 83(b) Election. The Participant acknowledges that he or she is responsible for obtaining the advice of the Participant's own tax advisors with respect to the award of RSUs and the Participant is relying solely on such advisors and not on any statements or representations of the Company or any of its agents with respect to the tax consequences relating to the RSUs. The Participant understands that the Participant (and not the Company) shall be responsible for the Participant's tax liability that may arise in connection with the acquisition, vesting and/or disposition of the RSUs. The Participant acknowledges that no election under Section 83(b) of the Internal Revenue Code of 1986, as amended, (the "Code") is available with respect to RSUs.

(b) Withholding. The Participant acknowledges and agrees that the Company has the right to deduct from payments of any kind otherwise due to the Participant any federal, state, local or other taxes of any kind required by law to be withheld with respect to the vesting of the RSUs. To the extent the Participant has not previously executed and delivered to the Company effective durable sell-to-cover instructions that by their terms would cover any taxes required by law to be withheld with respect to the vesting of the RSUs, at such time as the Participant is not aware of any material nonpublic information about the Company or the Common Stock and the Participant is not subject to any restriction on trading activities with respect to the Common Stock pursuant to any Company insider trading or other policy, the Participant shall execute the instructions set forth in Schedule A attached hereto (the "Durable Automatic Sell-to-Cover Instructions") as the means of satisfying such tax obligation. If the Participant has not executed the Durable Automatic Sell-to-Cover Instructions prior to an applicable vesting date, then the Participant agrees that if under applicable law the Participant will owe taxes at such vesting date on the portion of the award then vested the Company shall be entitled to immediate payment from the Participant of the amount of any tax required to be withheld by the Company. The Company shall not deliver any shares of Common Stock to the Participant until it is satisfied that all required withholdings have been made.

8. Miscellaneous.

(a) Section 409A. The RSUs awarded pursuant to this Agreement are intended to be exempt from or comply with the requirements of Section 409A of the Code and the Treasury Regulations issued thereunder ("Section 409A"). The delivery of shares of Common Stock on the vesting of the RSUs may not be accelerated or deferred unless permitted or required by Section 409A.

(b) Participant's Acknowledgements. The Participant acknowledges that he or she: (i) has read this Agreement; (ii) has been represented in the preparation, negotiation and execution of this Agreement by legal counsel of the Participant's own choice or has voluntarily declined to seek such counsel; (iii) understands the terms and consequences of this Agreement; (iv) is fully aware of the legal and binding effect of this Agreement; and (v) agrees that in accepting this award, the Participant will be bound by any clawback policy that the Company has adopted or may adopt in the future.

Schedule A

DURABLE AUTOMATIC SELL-TO-COVER INSTRUCTIONS

This Durable Automatic Sell-to-Cover Instruction (this "Instruction"), which is being delivered to Ocular Therapeutix, Inc. (the "Company") by the undersigned on the date set forth below (the "Adoption Date"), relates to the Covered RSUs (as defined following my signature below). This Instruction provides for "eligible sell-to-cover transactions" (as described in Rule 10b5-1(c)(1)(ii)(D)(3) under the Securities Exchange Act of 1934 (the "Exchange Act")) and is intended to satisfy the affirmative defense conditions of Rule 10b5-1(c)(1) under the Exchange Act.

I acknowledge that upon vesting and settlement of any Covered RSUs in accordance with the applicable RSU's terms, whether vesting is based on the passage of time or the achievement of performance goals, I will have compensation income equal to the fair market value of the shares of the Company's Common Stock subject to the RSUs that are settled on such settlement date and that the Company is required to withhold income and employment taxes in respect of that compensation income.

I desire to establish a plan and process to satisfy such withholding obligation in respect of all Covered RSUs through an automatic sale of a portion of the shares of the Company's Common Stock that would otherwise be issuable to me on each applicable settlement date, such portion to be in an amount sufficient to satisfy such withholding obligation, with the proceeds of such sale delivered to the Company in satisfaction of such withholding obligation.

I understand that the Company has arranged for the administration and execution of its equity incentive plans and the sale of securities by plan participants thereunder pursuant to a platform administered by a third party (the "Administrator") and the Administrator's designated brokerage partner.

Upon the settlement of any of my Covered RSUs pursuant to the Agreement after the 30th day following the Adoption Date (or if I am an officer of the Company on the Adoption Date, after the [later of: (i) the 90th day following the Adoption Date or (ii) two business days following the disclosure of the Company's financial results in Form 10-Q or Form 10-K for the completed fiscal quarter in which the Adoption Date occurs (or, with respect to this clause (ii), if sooner, the 120th day after the Adoption Date)][1] (the "Cooling-Off Period"), I hereby appoint the Administrator (or any successor administrator) to automatically sell such number of shares of the Company's Common Stock issuable with respect to such RSUs that vested and settled as is sufficient to generate net proceeds sufficient to satisfy the Company's minimum statutory withholding obligations with respect to the income recognized by me in connection with the vesting and settlement of such RSUs (based on minimum statutory withholding rates for all tax

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1 For a Participant who is a Section 16 officer of the Company, alternatively may insert "120th day following the Adoption Date".

purposes, including payroll and social security taxes, that are applicable to such income), and the Company shall receive such net proceeds in satisfaction of such tax withholding obligation.

I hereby appoint the Chief Executive Officer, the Chief Financial Officer and the Corporate Counsel, and any of them acting alone and with full power of substitution, to serve as my attorneys-in-fact to arrange for the sale of shares of the Company's Common Stock in accordance with this Instruction. I agree to execute and deliver such documents, instruments and certificates as may reasonably be required in connection with the sale of the shares of Common Stock pursuant to this Instruction.

Unless the third and final box in the definition of Covered RSUs below is checked, if I have previously adopted an automatic sale or sell-to-cover instruction relating to Covered RSUs, this Instruction shall be void *ab initio* with respect to such Covered RSUs.

I hereby certify that, as of the Adoption Date:

(i) I am not prohibited from entering into this Instruction by the Company's insider trading policy or otherwise;

(ii) I am not aware of any material nonpublic information about the Company or its Common Stock; and

(iii) I am adopting this Instruction in good faith and not as part of a plan or scheme to evade the prohibitions of Rule 10b-5 under the Exchange Act.

____

Print Name: _____________________

Date: __________________________

Covered RSUs:

The following restricted stock units ("RSUs") are covered by this Instruction.

Check all applicable boxes:

☐ The first award of RSUs granted to me on or after ______________ [*insert date of grant of current RSUs the grant of which is triggering the execution of this Instruction; if instruction is being executed in advance of a grant of RSUs, insert the Adoption Date*] and any RSUs that may, from time to time following such date, be granted to me by the Company, other than any future granted RSUs which by the terms of the applicable award agreement require the Company to withhold shares for tax withholding obligations in connection with the vesting and settlement of such RSUs, and therefore do not permit sell-to-cover transactions.

☐ Any outstanding RSUs that were granted to me by the Company prior to the Adoption Date that (1) are <u>not</u> subject to any prior automatic sale or sell-to-cover instruction and (2) for which the next vesting date is after the Cooling-Off Period, other than any previously granted RSUs which by the terms of the applicable award agreement require the Company to withhold shares for tax withholding obligations in connection with the vesting and settlement of such RSUs, and therefore do not permit sell-to-cover transactions.

☐ With respect to any RSUs, whether or not granted to me by the Company prior to the Adoption Date, that already are subject to an automatic sale or sell-to-cover instruction (a "Prior Instruction"), I elect to have such sales effected pursuant to this Instruction and confirm that doing so does not modify or change the amount, price, or timing of such sales from those provided by the Prior Instruction (and, as a result the Cooling-Off Period is not applicable to sales pursuant to this Instruction that were previously subject to the Prior Instruction).

Exhibit 10.42

EMPLOYMENT AGREEMENT

This EMPLOYMENT AGREEMENT (the "Agreement") sets forth the terms and conditions of your employment with Ocular Therapeutix, Inc., and will be effective as of February 22, 2024 (the "Effective Date"). In consideration of the mutual covenants contained in this Agreement, the Company and Executive agree as follows:

1. Employment. The Company agrees to employ Executive and Executive agrees to be employed by the Company on the terms and conditions set forth in this Agreement, effective as of the Effective Date.

(a) Capacity. Executive shall serve the Company as Chief Strategy Officer and shall have such duties and responsibilities as are customary for such position, reporting to the Company's Chief Executive Officer.

(a) Devotion of Duties; Representations. During the Term of Executive's employment with the Company, Executive shall devote 100% of Executive's best efforts and substantially all of Executive's business time and energies to the business and affairs of the Company and shall endeavor to perform the duties and services contemplated hereunder to the reasonable satisfaction of the Company. During the Term of Executive's employment with the Company, Executive shall not, without the prior written approval of the Company (by action of the Company's Chief Executive Officer (CEO)), undertake any other employment from any person or entity or serve as a director of any other company; provided, however, that (i) the Company will entertain requests as to such other employment or directorships in good faith and (ii) Executive will be eligible to participate in any outside activities permitted by a Company policy that is applicable to employees of the Company who are at the Vice President level or above and approved by the CEO after the date hereof; and provided further that in no event may any employment, directorship or outside activity be undertaken if it would (x) be in violation of any provision of this Agreement or other agreement between Executive and the Company, (y) interfere with the performance of Executive's duties for the Company, or (z) present a conflict of interest with the Company's business interests. Executive's normal place of work will be remote in Pennsylvania. However, Executive agrees to travel, at the Company's expense, on any business of the Company as may be reasonably required for the performance of Executive's duties. Executive agrees to abide by the rules, regulations, instructions, personnel practices and policies of the Company and any changes therein that may be adopted from time to time by the Company as provided in writing to Executive and applicable to senior executives of the Company. Notwithstanding anything to the contrary, Executive is allowed to engage in professional, educational, religious, civic, charitable, community and/or similar activities, and/or to manage his and/or his family's personal investments and affairs, provided that these activities do not interfere with or conflict with the performance of Executive's responsibilities under this Agreement.

2. Term of Employment.

(a) Executive's employment hereunder shall commence as of the Effective Date. Executive shall be employed at-will, meaning that, subject to the provisions of this Agreement, either the Company or Executive may terminate Executive's employment at any time for any legal reason.

(b) Notwithstanding, Executive's employment hereunder shall automatically be terminated upon the first to occur of the following:

(i) Immediately upon Executive's death;

(ii) By the Company, by written notice to Executive effective as of the date of such notice (or on such other date as specified in such notice):

(A) Following the Disability of Executive. "Disability" means that Executive is unable to perform his duties hereunder by reason of any mental, physical or other disability for a period of at least three (3) months, as determined by a qualified physician. Notwithstanding the foregoing, for any payments or benefits hereunder or pursuant to any other agreement between the Company and Executive, in either case that are subject to Section 409A of the Internal Revenue Code of 1986, as amended (the "Code") and the guidance issued thereunder, such Disability must result in Executive becoming "Disabled" within the meaning of Section 409A(a)(2)(C). (In this Agreement we refer to Section 409A of the Code and any guidance issued thereunder as "Section 409A."); or

(B) For Cause (as defined below); or

(C) Without Cause;

(iii) By Executive:

(A) At any time by written notice to the Company, effective thirty (30) days after the date of such notice, which notice period the Company may waive in whole or in part at its sole discretion; or

(B) By written notice to the Company for Good Reason (as defined below), effective on the date specified in such notice.

The period of Executive's employment by the Company under this Agreement is referred to herein as the "Term."

(c) Definition of "Cause". For purposes of this Agreement, "Cause" shall, pursuant to the reasonable good faith determination by the Company as documented in writing within 30-days of the Company's knowledge of one of the following, mean (i) the willful and continued failure by Executive to substantially perform Executive's material duties or responsibilities under this Agreement (other than such a failure as a result of Disability); (ii) any action or omission by Executive involving willful misconduct or gross negligence with regard to the Company, which has a detrimental effect on the Company; (iii) Executive's conviction of a felony, either in connection with the performance of Executive's obligations to the Company or which otherwise shall adversely affect Executive's ability to perform such obligations or shall materially adversely affect the business activities, reputation, goodwill or image of the Company; (iv) the material breach of a fiduciary duty to the Company; or (v) the material breach by Executive of any of the material provisions of this Agreement or the Restrictive Covenants Agreement (as defined below). In respect of the events described in clauses (i), (ii), (iv) and (v) above, the Company shall give Executive written notice of the failure of performance or breach, reasonable as to time, place and manner in the circumstances, and a 30-day opportunity to cure, provided that such failure of performance or breach is reasonably amenable to cure as determined by the Company in its sole discretion. Further, no Cause shall exist unless the Company has in good faith notified Executive of the alleged Cause condition in writing within 30-days of the Company's knowledge of the alleged Cause condition.

(d) Definition of "Good Reason". For purposes of this Agreement, a "Good Reason" shall mean any of the following, unless (i) the basis for such Good Reason is cured within a reasonable period of time (determined in the light of the cure appropriate to the basis of such Good Reason, but in no event less than thirty (30) after the Company receives written notice (which must be received from Executive within ninety (90) days of the initial existence of the condition giving rise to such Good Reason) specifying the basis for such Good Reason or (ii) Executive has consented in writing to the condition that would otherwise be a basis for Good Reason. Further, Executive needs to resign within 30 days after the Company has failed to cure the Good Reason(s):

(i) A change required by the Company in the principal location at which Executive provides services to the Company to a location more than fifty (50) miles from such principal location (which change, the Company has reasonably determined as of the date hereof, would constitute a material change in the geographic location at which Executive provides services to the Company); provided that such a relocation shall not be deemed to occur under circumstances where Executive's responsibilities require him to work at a location other than Executive's principal location for a reasonable period of time.

(ii) A material adverse change by the Company in Executive's duties, authority or responsibilities which causes Executive's position with the Company to become of materially less responsibility or authority than Executive's position immediately following Executive's first day of employment with the Company (the "Commencement Date") where such change is not remedied within ten (10) business days after written notice thereof by Executive;

(iii) A material reduction in Executive's base salary; or

(iv) A material breach of this Agreement by the Company which has not been cured within thirty (30) days after written notice thereof by Executive, which shall include, but not be limited to, the requirement for Executive to report to someone junior than the Company's Chief Executive Officer or the failure of the Company to comply with its financial obligations to Executive as set forth in this Agreement.

(e) Definition of "Corporate Change". For purposes of this Agreement, "Corporate Change" shall mean the occurrence of any of the following events:

(i) the acquisition by an individual, entity or group (within the meaning of Section 13(d)(3) or 14(d)(2) of the Securities Exchange Act of 1934, as amended (the "Exchange Act")) (a "Person") of beneficial ownership of any capital stock of the Company if, after such acquisition, such Person beneficially owns (within the meaning of Rule 13d-3 under the Exchange Act) more than 50% of either (x) the then-outstanding shares of common stock of the Company (the "Outstanding Company Common Stock") or (y) the combined voting power of the then-outstanding securities of the Company entitled to vote generally in the election of directors (the "Outstanding Company Voting Securities"); provided, however, that for purposes of this Section 2(e) the following acquisitions shall not constitute a Corporate Change: A) any acquisition directly from the Company or (B) any acquisition by any entity pursuant to a Business Combination (as defined below) which complies with clauses (x) and (y) of Section 2(e)(iii) of this definition;

(ii) a change in the composition of the Board that results in the Continuing Directors (as defined below) no longer constituting a majority of the Board (or, if applicable, the Board of Directors of a successor corporation to the Company), where the term "Continuing Director" means at any date a member of the Board (x) who was a member of the Board on the date of hereof or (y) who was nominated or elected subsequent to such date by at least a majority of the directors who were Continuing Directors at the time of such nomination or election or whose election to the Board was recommended or endorsed by at least a majority of the directors who were Continuing Directors at the time of such nomination or election; provided, however, that there shall be excluded from this clause (y) any individual whose initial assumption of office occurred as a result of an actual or threatened election contest with respect to the election or removal of directors or other actual or threatened solicitation of proxies or consents, by or on behalf of a person other than the Board; or

(iii) the consummation of a merger, consolidation, reorganization, recapitalization or share exchange involving the Company or a sale or other disposition of all or substantially all of the assets of the Company (a "Business Combination"), unless, immediately following such Business Combination, each of the following two conditions is satisfied: (x) the Outstanding Company Common Stock and Outstanding Company Voting Securities immediately prior to such Business Combination represent more than 50% of the then-outstanding shares of common stock or other common equity and the combined voting power of the then-outstanding securities entitled to vote generally in the election of directors or other governing body, respectively, of the resulting or acquiring entity in such Business Combination (which shall include, without limitation, a corporation which as a result of such transaction owns the Company or substantially all of the Company's assets either directly or through one or more subsidiaries) (such resulting or acquiring entity is referred to herein as the "Acquiring Entity") and (y) no Person (excluding any employee benefit plan (or related trust) maintained or sponsored by the Company or by the Acquiring Entity) beneficially owns, directly or indirectly, 50% or more of the then-outstanding shares of common stock of the Acquiring Entity, or of the combined voting power of the then-outstanding securities of such entity entitled to vote generally in the election of directors or other governing body (except to the extent that such ownership existed prior to the Business Combination).

Notwithstanding the foregoing, a "Corporate Change" shall not occur as a result of a Business Combination after which a majority of the Board of the Acquiring Entity consists of persons who were directors of the Company immediately prior to the Business Combination. For any payments or benefits hereunder (including pursuant to Section 4(b) hereof) or pursuant to any other agreement between the Company and Executive, in either case that are subject to Section 409A, the Corporate Change must constitute a "change in control event" within the meaning of Treasury Regulation Section 1.409A-3(i)(5)(i).

(f) Resignation from Other Positions. If, as of the date that Executive's employment terminates for any reason, Executive is a member of the Board (or the board of directors of any entity affiliated with the Company), or holds any other offices or positions with the Company (or any entity affiliated with the Company), Executive shall, unless otherwise requested by the Company, immediately relinquish and/or resign from any such board memberships, offices and positions as of the date Executive's employment terminates. Executive agrees to execute such documents and take such other actions as the Company may reasonably request to reflect such relinquishments and/or resignation(s).

3. Compensation.

(a) Base Salary. Executive's base salary during the Term shall be at the rate of at least $448,000.00 per year. Executive's base salary shall be payable in substantially equal installments in accordance with the Company's payroll practices as in effect from time to time, less any amounts required to be withheld under applicable law. Executive's base salary shall be reviewed annually for increase (but shall not be decreased).

(b) Bonus. In addition to the base salary, the Company may pay Executive an annual bonus (the "Bonus") as reasonably determined by the Board in good faith, solely in its reasonable and good faith discretion (it being understood that Executive's target annual bonus shall be 45% of Executive's base salary for such year and that payment of the Bonus shall be based on achievement of goals mutually set by the Company and Executive for the performance year. The Board's decision to issue a Bonus to Executive in any particular year shall have no effect on the discretion of the Board to grant or not to grant a Bonus in subsequent years. Executive must be an active employee of the Company as of December 31 of the relevant calendar year in order to be eligible for and to earn any Bonus for that year. Any Bonus for a particular year shall be paid or provided to Executive in a lump sum no later than March 15th of the calendar year following the calendar year in which the Bonus was approved by the Board and earned.

(c) Vacation. Executive shall be eligible to take up to 20 days of paid vacation during each year of the Term, subject to the accrual described in the following sentence, to be taken at such time or times as shall be mutually convenient and consistent with Executive's duties and obligations to the Company. The number of vacation days for which Executive is eligible shall accrue at the rate of 1.67 days per month. Vacation is at all times subject to the Company's Time-Off Policy, which the Company may change periodically in its sole discretion, provided that it does so for employees similarly situated to Executive and provided that in no event shall the amount of Executive's annual paid vacation days be reduced.

(d) Equity. As a material inducement to Executive entering into employment with the Company and In consideration of Executive's agreement in Section 5 to adhere to the non-competition provisions set forth in the Restrictive Covenants Agreement (as defined below), the Company shall grant to Executive, under the Company's 2019 Inducement Stock Incentive Plan, as amended (the "Plan"), (i) stock options to purchase 244,550 shares of the Company's common stock (the "Options") and (ii) a restricted stock unit award with respect to 80,300 shares of the Company's common stock (the "RSU"). The Options will have an exercise price per share equal to the last reported sale price per share of the common stock on the Nasdaq stock exchange on the grant date of the Option, will be a non-qualified stock option for United States tax purposes, will vest as to 25% of the underlying shares on the first anniversary of the Commencement Date and with respect to the balance of the underlying shares in 36 equal monthly installments thereafter and will otherwise be subject to the terms and conditions of a stock option agreement and the Plan.

The RSU will vest in equal quarterly installments beginning on the Commencement Date and ending on the third anniversary of the Commencement Date and will otherwise be subject to the terms and conditions of an RSU agreement and the Plan. The Options and the RSU shall be granted under the Plan as an “inducement grant” with the meaning of Nasdaq Listing Rule 5635(c)(4). Further, following the end of each fiscal year during the Term, and subject to the approval of the Board, which shall not be unreasonably withheld, Executive may be eligible for an equity award or awards, which will be based on both individual and corporate performance during the applicable fiscal year and such other factors as may be determined by the Board, in its sole discretion, and will be made under such terms and in such amounts as may be determined by the Board, in its sole discretion. Such individual and corporate performance goals will be mutually set by the Company and Executive for the performance year, and Executive shall be treated no less favorably than other senior executive officers of the Company who report to the Chief Executive Officer with respect to eligibility for future equity awards based in whole or part on corporate performance. In any event, Executive must be an active employee of the Company (and having neither received, nor been provided with, notice of termination) terminated for Cause on the date the equity award is granted in order to be eligible to receive a grant, as the grant also serves as an incentive to remain employed by the Company.

(e) Fringe Benefits. Executive shall be entitled to participate in any employee benefit plans that the Company makes available to its executives (including, without limitation, group life, disability, medical, dental and other insurance, retirement, pension, profit-sharing and similar plans) (collectively, the “Fringe Benefits”), provided that the Fringe Benefits shall not include any equity awards granted by the Company. These Fringe Benefits may be discontinued, modified or changed from time to time at the sole discretion of the Company, as long as Executive is treated no less favorably than similarly situated employees with respect to such changes. Where a particular Fringe Benefit is subject to a formal plan (for example, medical or life insurance), eligibility to participate in and receive any particular Fringe Benefit is governed solely by the applicable plan document, and eligibility to participate in such plan(s) may be dependent upon, among other things, a physical examination, subject to applicable law.

(f) Reimbursement of Expenses/Legal Fees. During the Term, Executive shall be entitled to reimbursement for all ordinary and reasonable out-of-pocket business expenses that are reasonably incurred by Executive in furtherance of the Company’s business in accordance with its policies for senior executives, subject to Section 4(d)(v). In addition, the Company shall either reimburse the Executive for, or pay directly for, legal fees he reasonably incurs in connection with this Agreement and any related agreements, not to exceed $10,000. Such reimbursement or payment shall be made within thirty (30) days after the Company's receipt of the invoice reflecting such legal fees, which reimbursement shall be reduced by applicable taxes and other withholdings.

(g) Indemnification. Executive shall be covered by all applicable indemnification and expense advancement policies of the Company applicable to senior executive officers generally and shall also be covered by the directors’ and officers’ liability insurance policy applicable to senior executive officers of the Company. For avoidance of doubt, the Company represents that it shall maintain directors’ and officers’ liability insurance for executive officers of the Company. For the avoidance of doubt, the provisions of this Section 3(g) shall survive the Executive’s separation of employment irrespective of the reason for such separation. Nothing in this Agreement shall limit Executive’s entitlements to indemnification, advancement, contribution and/or defense pursuant to any other written agreement with Company under which Executive is a beneficiary and/or applicable law.

(h) Clawback Policy. Executive agrees to be subject to, and bound by, the terms and conditions of the Company's Clawback Policy (as it may be amended, restated, supplemented, or otherwise modified from time to time, the "Policy"), a copy of which has been provided to or made available me. In the event it is determined in accordance with the Policy that any compensation or compensatory award granted, earned, or paid to Executive must be forfeited or reimbursed to the Company, Executive will promptly take any action necessary to effectuate such forfeiture and/or reimbursement as determined by the Company.

4. Special Termination Benefit.

(a) In the event of any termination of Executive's employment for any reason, the Company shall pay Executive (or Executive's estate) such portion of Executive's base salary as have accrued prior to such termination and have not yet been paid, together with (i) any amounts for expense reimbursement which have been properly incurred or the Company has become obligated to pay prior to termination and have not been paid as of the date of such termination, (ii) the amount of any Bonus previously granted to Executive by the Board but not yet paid, which amount shall not include any pro rata portion of any Bonus which would have been earned if such termination had not occurred; and (iii) payment for Executive's accrued unused vacation days (the "Accrued Obligations"). Such Accrued Obligations shall be paid as soon as possible after termination, and in any event in accordance with applicable law.

(b) In the event that Executive's employment hereunder is terminated (i) by Executive for Good Reason or (ii) by the Company without Cause (a "Qualifying Termination"), the Company shall pay to Executive the Accrued Obligations and shall make the severance payments and provide the benefits described below; provided that receipt of any such severance payments and benefits (other than the Accrued Obligations) shall be dependent upon Executive's execution and, to the extent applicable, non-revocation of a separation and general release of claims agreement in substantially the form attached hereto as Exhibit A (which may be revised by the Company in accordance with the footnotes therein) (the "Release"), provided to Executive in connection with Executive's termination. The Release must be signed and any applicable revocation period with respect thereto must have expired by the sixtieth (60th) day following Executive's termination of employment. The severance payments and benefits shall be paid or commence, as applicable, on the first payroll period following the date of the Executive's termination and an effective Release (the "Payment Date"). Notwithstanding the foregoing, if the 60th day following Executive's termination occurs in the calendar year following the date on which Executive's employment terminates, the Payment Date shall be no earlier than January 1 of such subsequent calendar year.

(i) If Executive's Qualifying Termination occurs, the Company shall continue to pay Executive's highest base salary from the last two years for twelve (12) months following Executive's termination of employment in accordance with the Company's payroll practice and less applicable taxes and withholdings, beginning on the Payment Date; provided, that the first installment will include all amounts that otherwise would have been paid to Executive from the date Executive's employment terminates through the Payment Date had the Release become effective on the date of termination. If

Executive's Qualifying Termination occurs during the period commencing on the date ninety (90) days prior to the closing of a Corporate Change and ending twelve (12) months following a Corporate Change (the "Protected Period"), then, in lieu of the foregoing, the Company shall pay Executive eighteen (18) months of Executive's base salary in a lump sum on the Payment Date, less applicable taxes and withholdings. In the event of a Qualifying Termination during the Protected Period that occurs prior to the occurrence of a Corporate Change such that the Payment Date occurs prior to the occurrence of the Corporate Change, (x) following the occurrence of the Corporate Change, the Company shall pay Executive the Protected Period severance amount following the Corporate Change, less any severance payments made previously under the clause and (y) if necessary to comply with the provisions of Code Section 409A (as defined below) certain severance payments shall continue to be made in installments. The Company shall promptly inform Executive in writing of a Corporate Change that closes during the one-year period following a Qualifying Termination.

(ii) Only if the Qualifying Termination occurs during the Protected Period, the Company shall pay Executive an amount equal to one and one-half times Executive's target annual bonus, described in Section 3(b) hereof, for the year in which the termination of employment occurs, which total amount shall be payable in a lump sum on the Payment Date, less applicable taxes and withholdings.

(iii) If the Qualifying Termination occurs during the Protected Period, any equity grants that vest solely based on Executive's continued performance of services shall become fully vested, exercisable and nonforfeitable as of the effective date of the Release (the "Acceleration Date"). For the avoidance of doubt, any equity awards that vest based on the achievement of performance metrics shall be governed by the terms of the applicable award agreement and shall not be entitled to accelerated vesting pursuant to this Agreement.

(iv) Should Executive timely elect and be eligible to continue receiving group medical coverage pursuant to the law known as COBRA, and so long as the Company can provide such benefit without violating the nondiscrimination requirements of applicable law, the Company will pay the share of the premiums for such coverage for Executive and any dependents to maintain group medical, dental, prescription drug, and/or vision insurance benefits at no less than the coverage levels in effect as of the day before Executive's last day of employment as well as any administrative fee, for twelve (12) months following Executive's termination of employment (or, if the Qualifying Termination occurs during the Protected Period, for eighteen (18) months following such termination of employment), subject to applicable law and the terms of the respective policies; provided that the Company's obligation to provide the premium payments contemplated herein shall terminate upon Executive becoming eligible for coverage under the medical benefits program of a subsequent employer.. The foregoing shall not be construed to extend any period of continuation coverage (e.g., COBRA) required by Federal law.

(c) Except as otherwise set forth in this Agreement and/or other written agreements between the Company and Executive, the Company shall have no obligation to pay Executive (or Executive's estate) any other compensation or provide any other benefit(s) following such termination except as provided in this Section 4.

(d) Compliance with Section 409A. Subject to the provisions in this Section 4(d), any severance payments or benefits under this Agreement shall begin only upon the date of Executive's "separation from service" (determined as set forth below) which occurs on or after the date of termination of Executive's employment. The following rules shall apply with respect to the distribution of the severance payments and benefits, if any, to be provided to Executive under this Agreement:

(i) It is intended that each installment of the severance payments and benefits provided under this Agreement shall be treated as a separate "payment" for purposes of Section 409A. Neither the Company nor Executive shall have the right to accelerate or defer the delivery of any such payments or benefits except to the extent specifically permitted or required by Section 409A.

(ii) If, as of the date of Executive's "separation from service" from the Company, Executive is not a "specified employee" (within the meaning of Section 409A), then each installment of the severance payments and benefits shall be made on the dates and terms set forth in this Agreement.

(iii) If, as of the date of Executive's "separation from service" from the Company, Executive is a "specified employee" (within the meaning of Section 409A), then:

(A) Each installment of the severance payments and benefits due under this Agreement that, in accordance with the dates and terms set forth herein, will in all circumstances, regardless of when the separation from service occurs, be paid within the short-term deferral period (as defined under Section 409A) shall be treated as a short-term deferral within the meaning of Treasury Regulation Section 1.409A-1(b)(4) to the maximum extent permissible under Section 409A and such payments and benefits shall be paid or provided on the dates and terms set forth in this Agreement; and

(B) Each installment of the severance payments and benefits due under this Agreement that is not described in Section 4(d)(iii)(A) above and that would, absent this subsection (B), be paid within the six-month period following Executive's "separation from service" from the Company shall not be paid until the date that is six months and one day after such separation from service (or, if earlier, Executive's death), with any such installments that are required to be delayed being accumulated during the six-month period and paid in a lump sum on the date that is six months and one day following Executive's separation from service and any subsequent installments, if any, being paid in accordance with the dates and terms set forth herein; provided, however, that the preceding provisions of this sentence shall not apply to any installment of severance payments and benefits if and to the maximum extent that such installment is deemed to be paid under a separation pay plan that does not provide for a deferral of compensation by reason of the application of Treasury Regulation 1.409A-1(b)(9)(iii) (relating to separation pay upon an involuntary separation from service). Any installments that qualify for the exception under Treasury

Regulation Section 1.409A-1(b)(9)(iii) must be paid no later than the last day of Executive's second taxable year following the taxable year in which the separation from service occurs.

(iv) The determination of whether and when Executive's separation from service from the Company has occurred shall be made in a manner consistent with, and based on the presumptions set forth in, Treasury Regulation Section 1.409A-1(h). Solely for purposes of this Section 4(d)(iv), "Company" shall include all persons with whom the Company would be considered a single employer under Sections 414(b) and 414(c) of the Code.

(v) All reimbursements and in-kind benefits provided under this Agreement shall be made or provided in accordance with the requirements of Section 409A to the extent that such reimbursements or in-kind benefits are subject to Section 409A, including, where applicable, the requirements that (i) any reimbursement is for expenses incurred during Executive's lifetime (or during a shorter period of time specified in this Agreement), (ii) the amount of expenses eligible for reimbursement during a calendar year may not affect the expenses eligible for reimbursement in any other calendar year, (iii) the reimbursement of an eligible expense will be made on or before the last day of the calendar year following the year in which the expense is incurred and (iv) the right to reimbursement is not subject to set off or liquidation or exchange for any other benefit.

(vi) Notwithstanding anything herein to the contrary, the Company shall have no liability to Executive or to any other person if the payments and benefits provided hereunder that are intended to be exempt from or compliant with Section 409A are not so exempt or compliant.

(e) Modified Section 280G Cutback.

(i) Notwithstanding any other provision of this Agreement, except as set forth in Section 4(e)(ii), in the event that the Company undergoes a "Change in Ownership or Control" (as defined below), the Company shall not be obligated to provide to Executive a portion of any "Contingent Compensation Payments" (as defined below) that Executive would otherwise be entitled to receive to the extent necessary to eliminate any "excess parachute payments" (as defined in Section 280G(b)(1) of the Code) for Executive. For purposes of this Section 4(e), the Contingent Compensation Payments so eliminated shall be referred to as the "Eliminated Payments" and the aggregate amount (determined in accordance with Treasury Regulation Section 1.280G-1, Q/A-30 or any successor provision) of the Contingent Compensation Payments so eliminated shall be referred to as the "Eliminated Amount."

(ii) Notwithstanding the provisions of Section 4(e)(i), no such reduction in Contingent Compensation Payments shall be made if (1) the Eliminated Amount (computed without regard to this sentence) exceeds (2) 100% of the aggregate present value (determined in accordance with Treasury Regulation Section 1.280G-1, Q/A-31 and Q/A-32 or any successor provisions) of the amount of any additional taxes that would be incurred by Executive if the Eliminated Payments (determined without regard to this sentence) were paid to Executive (including federal and state income taxes on the Eliminated Payments, the excise tax imposed by Section 4999 of the Code payable with respect to all of the Contingent Compensation Payments in excess of Executive's "base amount" (as defined in Section 280G(b)(3) of the Code), and any withholding taxes). The override of such reduction in Contingent Compensation Payments pursuant to this Section 4(e)(ii) shall be referred to as a "Section 4(e)(ii) Override." For purpose of this paragraph, if any federal or state income taxes would be attributable to the receipt of any Eliminated Payment, the amount of such taxes shall be computed by multiplying the amount of the Eliminated Payment by the maximum combined federal and state income tax rate provided by law.

(iii) For purposes of this Section 4(e) the following terms shall have the following respective meanings:

(A) "Change in Ownership or Control" shall mean a change in the ownership or effective control of the Company or in the ownership of a substantial portion of the assets of the Company determined in accordance with Section 280G(b)(2) of the Code.

(B) "Contingent Compensation Payment" shall mean any payment (or benefit) in the nature of compensation that is made or made available (under this Agreement or otherwise) to a "disqualified individual" (as defined in Section 280G(c) of the Code) and that is contingent (within the meaning of Section 280G(b)(2)(A)(i) of the Code) on a Change in Ownership or Control of the Company.

(iv) Any payments or other benefits otherwise due to Executive following a Change in Ownership or Control that could reasonably be characterized (as determined by the Company) as Contingent Compensation Payments (the "Potential Payments") shall not be made until the dates provided for in this Section 4(e)(iv). Within 30 days after each date on which Executive first becomes entitled to receive (whether or not then due) a Contingent Compensation Payment relating to such Change in Ownership or Control, the Company shall notify Executive (with reasonable detail regarding the basis for its determinations) (1) which Potential Payments constitute Contingent Compensation Payments, (2) the Eliminated Amount and (3) whether the Section 4(e)(ii) Override is applicable. Within 30 days after delivery of such notice to Executive, Executive shall deliver a response to the Company (the "Executive Response") stating either (A) that Executive agrees with the Company's determination pursuant to the preceding sentence or (B) that Executive disagrees with such determination, in which case Executive shall set forth (x) which Potential Payments should be characterized as Contingent Compensation Payments, (y) the Eliminated Amount, and (z) whether the Section 4(e)(ii) Override is applicable. In the event that Executive fails to deliver an Executive Response on or before the required date, the Company's initial determination shall be final. If Executive states in the Executive Response that Executive agrees with the Company's determination, the Company shall make the Potential Payments to Executive within three business days following delivery to the Company of the Executive Response (except for any Potential Payments which are not due to be made until after such date, which Potential Payments shall be made on the date on which they are due). If Executive states in the Executive Response that Executive disagrees with the Company's determination, then, for a period of 60 days following delivery of the Executive Response, Executive and the Company shall use good faith efforts to resolve such dispute. If such dispute is not resolved within such 60-day period, such dispute shall be settled exclusively by arbitration in the greater Boston, Massachusetts area, in accordance with the rules of the American Arbitration Association then in effect. Judgment may be entered on the arbitrator's award in any court having jurisdiction. The

Company shall, within three business days following delivery to the Company of the Executive Response, make to Executive those Potential Payments as to which there is no dispute between the Company and Executive regarding whether they should be made (except for any such Potential Payments which are not due to be made until after such date, which Potential Payments shall be made on the date on which they are due). The balance of the Potential Payments shall be made within three business days following the resolution of such dispute.

(v) The Contingent Compensation Payments to be treated as Eliminated Payments shall be determined by the Company by determining the "Contingent Compensation Payment Ratio" (as defined below) for each Contingent Compensation Payment and then reducing the Contingent Compensation Payments in order beginning with the Contingent Compensation Payment with the highest Contingent Compensation Payment Ratio. For Contingent Compensation Payments with the same Contingent Compensation Payment Ratio, such Contingent Compensation Payment shall be reduced based on the time of payment of such Contingent Compensation Payments with amounts having later payment dates being reduced first. For Contingent Compensation Payments with the same Contingent Compensation Payment Ratio and the same time of payment, such Contingent Compensation Payments shall be reduced on a pro rata basis (but not below zero) prior to reducing Contingent Compensation Payments with a lower Contingent Compensation Payment Ratio. The term "Contingent Compensation Payment Ratio" shall mean a fraction the numerator of which is the value of the applicable Contingent Compensation Payment that must be taken into account by Executive for purposes of Section 4999(a) of the Code, and the denominator of which is the actual amount to be received by Executive in respect of the applicable Contingent Compensation Payment. For example, in the case of an equity grant that is treated as contingent on the Change in Ownership or Control because the time at which the payment is made or the payment vests is accelerated, the denominator shall be determined by reference to the fair market value of the equity at the acceleration date, and not in accordance with the methodology for determining the value of accelerated payments set forth in Treasury Regulation Section 1.280G-1Q/A-24(b) or (c)).

(vi) The provisions of this Section 4(e) are intended to apply to any and all payments or benefits available to Executive under this Agreement or any other agreement or plan of the Company under which Executive receives Contingent Compensation Payments.

5. Proprietary Rights, Inventions, Non-Competition and Non-Solicitation Agreement.

Executive acknowledges and agrees that Executive must, as a condition of Executive's employment, execute, within ten (10) business days following Executive's Commencement Date (but in no event prior to the Commencement Date), the Proprietary Rights, Inventions, Non-Competition and Non-Solicitation Agreement attached hereto as Exhibit B (the "Restrictive Covenants Agreement") indicating Executive's agreement to all of Executive's obligations thereunder. Executive further acknowledges that the Executive's receipt of the equity awards as set forth in Section 3(d) above and Executive's eligibility for the severance benefits described in Section 4(b) above is contingent on Executive's agreement to the post-employment non-competition provisions set forth in the Restrictive Covenants Agreement. Executive further acknowledges that such consideration was mutually agreed upon by Executive and the Company and is fair and reasonable in exchange for Executive's compliance with such non-competition obligations and that Executive was provided at least ten (10) business days to review the Restrictive Covenants Agreement.

6. Records. Upon termination of Executive's relationship with the Company, Executive shall deliver to the Company any property of the Company which may be in Executive's possession including products, materials, memoranda, notes, records, reports, or other documents or photocopies of the same, except as provided in the Restrictive Covenant Agreement and provided that electronic information may be destroyed rather than returned. Further, for avoidance of doubt, Executive shall be entitled to retain and use contact information, whether in hard copy or electronic format, and Executive's own personnel and/or compensation information.

7. No Conflicting Agreements; Representations; Disclosure of Employment.

(a) Executive hereby represents and warrants that Executive has no commitments or obligations inconsistent with this Agreement and Executive's employment hereunder. Executive further represents and warrants that no conflict of interest exists as between this Agreement and any other agreement to which Executive is a party, that there are no other lawful restrictions of any kind with respect to Executive's employment with the Company and the acceptance of related compensation and that Executive will not enter into any agreement or other arrangements during the Term which will result in a conflict of interest or such other restrictions. Executive will keep the Company informed of any changes in circumstance that could lead to a conflict of interest between Executive and the Company and if in doubt, Executive will inform the Company to ascertain if there is an unacceptable conflict to the Company.

(b) Executive hereby represents that Executive is not bound by the terms of any agreement with any third party, to refrain from competing, directly or indirectly, with the business of such third party or to refrain from soliciting employees, customers or suppliers of such third party. Executive further represents that Executive will not disclose to the Company or induce the Company to use any confidential or proprietary information or material belonging to any current or previous employer or others.

8. Conditions to Employment. Executive shall, from time to time during employment as determined by the Company in its sole discretion, be available for and cooperate with the Company in obtaining background checks on Executive, including providing any and all consents necessary to the accomplishment of the foregoing, as required by law or to comply with Company policies. Executive's employment is also conditioned on Executive's provision of proof of Executive's identity and right to work in the United States, as required by federal law.

9. General.

(a) Notices. All notices, requests, consents and other communications hereunder shall be in writing, shall be addressed to the receiving party's address as follows:

If to the Company:

Ocular Therapeutix, Inc.
24 Crosby Drive
Bedford, MA 01730
USA
Attention: VP, Human Resources
Telephone: (781) 357-4000

With an email copy to:

VP, Human Resources: hr@ocutx.com
VP, Law Department: law@ocutx.com

If to Executive: Sanjay Nayak
113 Harvard Ln, Bryn Mawr, PA 19010

or to such other address as a party may designate by notice hereunder, and shall be either (i) delivered by hand, (ii) sent by overnight courier, or (iii) sent by registered or certified mail, return receipt requested, postage prepaid. All notices, requests, consents and other communications hereunder shall be deemed to have been given either (i) if by hand, at the time of the delivery thereof to the receiving party at the address of such party set forth above, (ii) if sent by overnight courier, on the next business day following the day such notice is delivered to the courier service, or (iii) if sent by registered or certified mail, on the fifth (5th) business day following the day such mailing is made.

(b) Entire Agreement. This Agreement, together with any referenced agreements incorporated herein, including the Restrictive Covenants Agreement and equity award agreements, embodies the entire agreement and understanding between the parties hereto with respect to the subject matter hereof and supersedes all prior oral or written agreements and understandings relating to the subject matter hereof. No statement, representation, warranty, covenant or agreement of any kind not expressly set forth in this Agreement shall affect, or be used to interpret, change or restrict, the express terms and provisions of this Agreement.

(c) Modifications and Amendments. The terms and provisions of this Agreement may be modified or amended only by written agreement executed by the parties hereto.

(d) Waivers and Consents. The terms and provisions of this Agreement may be waived, or consent for the departure therefrom granted, only by written document specifically denominated as such and executed by both parties. No such waiver or consent shall be deemed to be or shall constitute a waiver or consent with respect to any other terms or provisions of this Agreement, whether or not similar. Each such waiver or consent shall be effective only in the specific instance and for the purpose for which it was given, and shall not constitute a continuing waiver or consent.

(e) Assignment. The Company shall assign its rights and obligations hereunder to any person or entity that succeeds to all or substantially all of the Company's business or that aspect of the Company's business in which Executive is principally involved, on written advance notice to Executive. Executive may not assign Executive's rights and obligations under this Agreement without the prior written consent of the Company.

(f) Benefit. All statements, representations, warranties, covenants and agreements in this Agreement shall be binding on the parties hereto and shall inure to the benefit of the respective successors, estates, executors, heirs, and permitted assigns of each party hereto. Nothing in this Agreement shall be construed to create any rights or obligations except among the parties hereto, and no person or entity shall be regarded as a third-party beneficiary of this Agreement.

(g) Governing Law. This Agreement and the rights and obligations of the parties hereunder shall be construed in accordance with and governed by the law of the Commonwealth of Pennsylvania, without giving effect to the conflict of law principles thereof.

(h) Jurisdiction and Service of Process. Any legal action or proceeding with respect to this Agreement shall be brought in the courts of the Commonwealth of Pennsylvania or of the United States of America for the Eastern District of Pennsylvania. By execution and delivery of this Agreement, each of the parties hereto accepts for itself and in respect of its property, generally and unconditionally, the jurisdiction of the aforesaid courts. Each of the parties hereto irrevocably consents to the service of process of any of the aforementioned courts in any such action or proceeding by the mailing of copies thereof by certified mail, postage prepaid, to the party at its address set forth in Section 9(a) hereof.

(i) Severability. The parties intend this Agreement to be enforced as written. However, (i) if any portion or provision of this Agreement shall to any extent be declared illegal or unenforceable by a duly authorized court having jurisdiction, then the remainder of this Agreement, or the application of such portion or provision in circumstances other than those as to which it is so declared illegal or unenforceable, shall not be affected thereby, and each portion and provision of this Agreement shall be valid and enforceable to the fullest extent permitted by law.; and (ii) if any provision, or part thereof, is held to be unenforceable because of the duration of such provision or the geographic area covered thereby, the Company and Executive agree that the court making such determination shall have the power to reduce the duration and/or geographic area of such provision, and/or to delete specific words and phrases ("blue-penciling"), and in its reduced or blue-penciled form such provision shall then be enforceable and shall be enforced..

(j) Headings and Captions; Interpretation. The headings and captions of the various subdivisions of this Agreement are for convenience of reference only and shall in no way modify, or affect the meaning or construction of any of the terms or provisions hereof.

(k) No Waiver of Rights, Powers and Remedies. No failure or delay by a party hereto in exercising any right, power or remedy under this Agreement, and no course of dealing between the parties hereto, shall operate as a waiver of any such right, power or remedy of the party. No single or partial exercise of any right, power or remedy under this Agreement by a party hereto, nor any abandonment or discontinuance of steps to enforce any such right, power or remedy, shall preclude such party from any other or further exercise thereof or the exercise of any other right, power or remedy hereunder. The election of any remedy by a party hereto shall not constitute a waiver of the right of such party to pursue other available remedies. No notice to or demand on a party not expressly required under this Agreement shall entitle the party receiving such notice or demand to any other or further notice or demand in similar or other circumstances or constitute a waiver of the rights of the party giving such notice or demand to any other or further action in any circumstances without such notice or demand.

(l) Counterparts. This Agreement may be executed in one or more counterparts, and by different parties hereto on separate counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

(m) Survival. The provisions of Sections 3(f) and (g), 4, 6, and 9 shall survive the termination of this Agreement and Executive's employment hereunder in accordance with their terms. For the avoidance of doubt, the Restrictive Covenants Agreement shall also survive the termination of this Agreement and Executive's employment hereunder.

[*Remainder of Page Intentionally Left Blank*]

IN WITNESS THEREOF, the parties hereto have executed this Agreement as of the day and year first above written.

Ocular Therapeutix, Inc.

/s/ Antony Mattessich
Name: Antony Mattessich
Title: President and Chief Executive Officer

Agreed and Accepted

/s/ Sanjay Nayak
Name: Sanjay Nayak

EXHIBIT A TO EMPLOYMENT AGREEMENT[1]

VIA [HAND DELIVERY/ELECTRONIC MAIL]

[Insert Date]

[Insert Employee Name]
[Insert Employee Address]

Dear [Insert Employee Name]:

As we discussed, your employment with Ocular Therapeutics, Inc. (the "Company") [is ending][has ended] effective [insert separation date] (the "Separation Date"). As we also discussed, you will be eligible to receive the Severance Benefits described in Section 4(b) of the Employment Agreement dated [insert date] between you and the Company to which this letter agreement is attached as Exhibit A (the "Employment Agreement"), and referenced in paragraph 1 below, if you sign and return this letter agreement to me on or before [Insert Return Date at least 60 days from separation date[2]][, but no earlier than the Separation Date,] and do not revoke your agreement (as described below). By signing and returning this letter agreement and not revoking your acceptance, you will be entering into a binding agreement with the Company and will be agreeing to the terms and conditions set forth in the numbered paragraphs below, including the release of claims set forth in paragraph 2. Therefore, you are advised to consult with an attorney before signing this letter agreement [and you have been given at least [twenty-one (21)][forty-five (45) [3]] days to do so]. If you sign this letter agreement, you may change your mind and revoke your agreement during the seven (7) business day period after you have signed it (the "Revocation Period") by notifying [me] in writing. If you do not so revoke, this letter agreement will become a binding agreement between you and the Company upon the expiration of the Revocation Period.

Although your receipt of the Severance Benefits is expressly conditioned on your entering into this letter agreement, the following will apply regardless of whether or not you do so:

- As of the Separation Date, all salary payments from the Company will cease and any benefits you had as of the Separation Date under Company-provided benefit plans, programs, or practices will terminate, except as required by federal or state law and provided that your participation as an active employee in the Company's medical, dental, vision, and/or prescription drug insurance plans will terminate on your Separation Date.
- You will receive payment for your final wages and any unused vacation time accrued through the Separation Date.

[1] Note: You and the Company may mutually and in good faith reasonably revise this release to reflect changes in law, additional statutes or claims, benefits, , so that the Company receives the benefit of the most complete release of claims that is legally permissible (without releasing your right to receive the severance benefits set forth in the Employment Agreement). This footnote and the other footnotes herein are part of the form of release and are to be removed only when the Company finalizes the letter agreement for execution.
[2] Note: The period will be not less than 60 days.
[3] Note: The timing depends on your age at separation from employment, and whether the termination involves a group of employees.

- You may, if eligible and at your own cost, elect to continue receiving group medical insurance pursuant to the "COBRA" law. Please consult the COBRA materials to be provided under separate cover for details regarding these benefits. As described below, if you sign this letter agreement, the Company will continue to pay the share of COBRA costs described in Section 4(b) of the Employment Agreement.
- You are obligated to keep confidential and not to use or disclose any and all non-public information concerning the Company that you acquired during the course of your employment with the Company, including any non-public information concerning the Company's business affairs, business prospects, and financial condition, except as otherwise permitted by paragraph 4(c) below, your other agreements with the Company, and as required by law or governmental agency. Further, you remain subject to your continuing obligations to the Company as set forth in the Proprietary Rights, Inventions, Non-Competition and Non-Solicitation Agreement attached to the Employment Agreement as Exhibit B (the "Restrictive Covenants Agreement"), which remains in full force and effect.
- You must return to the Company no later than the Separation Date all Company property.
- Within 10 days, you will be reimbursed for all outstanding business expenses incurred as of the last day of your employment.

If you elect to timely sign and return this letter agreement and do not revoke your acceptance within the Revocation Period, the following terms and conditions will also apply:

1. **Severance Benefits** –The Company will provide you with the pay and benefits set forth in Section 4(b) of the Employment Agreement (the "Severance Benefits"), in accordance with and subject to the terms thereof. You will not be eligible for, nor shall you have a right to receive, any payments or benefits from the Company following the Separation Date other than as set forth in this paragraph and in the Employment Agreement and/or other written agreements with the Company.

2. **Release of Claims** – In consideration of the severance benefits, which you acknowledge you would not otherwise be entitled to receive, you hereby fully, forever, irrevocably and unconditionally release, remise and discharge the Company, its affiliates, subsidiaries, parent companies, predecessors, and successors, and all of their respective past and present officers, directors, stockholders, partners, members, employees, agents, representatives, plan administrators, attorneys, insurers and fiduciaries (each in their capacities as such) (collectively, the "Released Parties") from any and all claims, charges, complaints, demands, actions, causes of action, suits, rights, debts, sums of money, costs, accounts, reckonings, covenants, contracts, agreements, promises, doings, omissions, damages, executions, obligations, liabilities, and expenses (including attorneys' fees and costs), of every kind and nature that you ever had or now have against any or all of the Released Parties, whether known or unknown, including, but not limited to, any and all claims arising out of or relating to your employment with and/or separation from the Company, including, but not limited to, all claims under Title VII of the Civil Rights Act of 1964, 42 U.S.C. § 2000e et seq., the Americans With Disabilities Act of 1990, 42 U.S.C. § 12101 et seq., [the Age Discrimination in Employment Act, 29 U.S.C. § 621 et seq.], the Genetic Information Nondiscrimination Act of 2008, 42 U.S.C. § 2000ff et seq.,

the Family and Medical Leave Act, 29 U.S.C. § 2601 et seq., the Worker Adjustment and Retraining Notification Act ("WARN"), 29 U.S.C. § 2101 et seq., the Rehabilitation Act of 1973, 29 U.S.C. § 701 et seq., Executive Order 11246, Executive Order 11141, the Fair Credit Reporting Act, 15 U.S.C. § 1681 et seq., and the Employee Retirement Income Security Act of 1974 ("ERISA"), 29 U.S.C. § 1001 et seq., all as amended; all claims arising out of the Massachusetts Fair Employment Practices Act, Mass. Gen. Laws ch. 151B, § 1 et seq., the Massachusetts Civil Rights Act, Mass. Gen. Laws ch. 12, §§ 11H and 11I, the Massachusetts Equal Rights Act, Mass. Gen. Laws. ch. 93, § 102, Mass. Gen. Laws ch. 214, § 1C (Massachusetts right to be free from sexual harassment law), the Massachusetts Labor and Industries Act, Mass. Gen. Laws ch. 149, § 1 et seq., Mass. Gen. Laws ch. 214, § 1B (Massachusetts right of privacy law), the Massachusetts Parental Leave Act, Mass. Gen. Laws ch. 149, § 105D, and the Massachusetts Small Necessities Leave Act, Mass. Gen. Laws ch. 149, § 52D, all as amended; all rights and claims under the Massachusetts Wage Act, Mass. Gen. Laws ch. 149, § 148 et seq., as amended (Massachusetts law regarding payment of wages and overtime), including any rights or claims thereunder to unpaid wages, including overtime, bonuses, commissions, and accrued, unused vacation time; all common law claims including, but not limited to, actions in defamation, intentional infliction of emotional distress, misrepresentation, fraud, wrongful discharge, and breach of contract (including, without limitation, all claims arising out of or related to the Employment Agreement); all claims to any non-vested ownership interest in the Company, contractual or otherwise; all state and federal whistleblower claims to the maximum extent permitted by law; and any claim or damage arising out of your employment with and/or separation from the Company (including a claim for retaliation) under any common law theory or any federal, state or local statute or ordinance not expressly referenced above; provided, however, that this release of claims shall not (i) prevent you from filing a charge with, cooperating with, or participating in any investigation or proceeding before, the Equal Employment Opportunity Commission or a state fair employment practices agency (except that you acknowledge that you may not recover any monetary benefits in connection with any such charge, investigation, or proceeding, and you further waive any rights or claims to any payment, benefit, attorneys' fees or other remedial relief in connection with any such charge, investigation or proceeding), (ii) waive or deprive you of any rights you may have to indemnification, contribution, and/or defense pursuant to the Company's Articles of Incorporation and/or By-Laws, any existing written indemnification agreement between you and the Company (iii) waive any rights or claims arising after the date on which you sign this letter agreement, including the right to enforce this letter agreement, (iv) release claims that cannot be released as a matter of law; (v) release any rights or claims regarding COBRA, workers compensation, and/or unemployment insurance benefits (the application for which shall not be contested by the Company), (vi) release claims or rights regarding accrued, vested benefits under any employee benefit, stock, savings, insurance, the 2019 Inducement Stock Incentive Plan and/or awards issued pursuant to that Plan, other incentive compensation plan, and/or retirement, 401(k), pension plan of the Company, including, without limitation, vested stock options, vested restricted stock units, and/or vested 401(k) benefits; and/or (vii) release any rights regarding pending claims for medical, dental, vision, and/or prescription drug insurance benefits, which shall be governed by the terms of the applicable plan.

3. **Continuing Obligations** – You acknowledge and reaffirm your confidentiality and non-disclosure obligations discussed above in this letter agreement, as well as any applicable continuing obligations set forth in the Restrictive Covenants Agreement, which survive your separation from employment with the Company. In addition, as an express condition of your receipt of the severance benefits, you agree that, for a period of one (1) year following the Separation Date, you will not, in the Applicable Territory (as defined below), directly or indirectly, whether as an owner, partner, officer, director, employee, consultant, investor, lender or otherwise, except as the passive holder of not more than 1% of the outstanding stock of a publicly-held company, engage or assist others in engaging in any business or enterprise that is competitive with the Company's business in the ophthalmic space, including but not limited to any business or enterprise that researches, develops, manufactures, markets, licenses, sells or provides any product or service that competes with or is intended to compete with any product or service researched, developed, manufactured, marketed, licensed, sold or provided, or actively being planned to be researched, developed, manufactured, marketed, licensed, sold or provided by the Company in the ophthalmic space (a "Competitive Company"), if you would be performing job duties or services for the Competitive Company that are of a similar type that you performed for the Company at any time during the last two (2) years of your employment. As a senior leader for the Company, you acknowledge and agree that, in the performance of your duties for the Company (including without limitation, assisting the Company with its overall business strategy), you were involved in all aspects of the Company's business and operations. Accordingly, you acknowledge and agree that undertaking any leadership role in a Competitive Company would constitute performing job duties or services of a similar type that you performed for the Company. For purposes of this paragraph 3, "Applicable Territory" shall mean the geographic areas in which you provided services or had a material presence or influence at any time during your last two (2) years of your employment and, as a senior leader for the Company, you acknowledge that your duties and responsibilities required you to have a material presence and/or influence anywhere that the Company does business, but in any event shall be limited to the United States. Notwithstanding the foregoing, this paragraph 3 shall not preclude you from becoming an employee of, or from otherwise providing services to, a separate division or operating unit of a multi-divisional Competitive Company (a "Division") if: (i) the Division by which you are employed, or to which the you provide services, is not competitive with the Company's business (within the meaning of this paragraph 3), and (ii) you do not provide services, directly or indirectly, to any other division or operating unit of such multi-divisional Competitive Company that is competitive with the Company's business (within the meaning of this paragraph 3). If any restriction set forth in this paragraph is found by any court of competent jurisdiction to be unenforceable because it extends for too long a period of time or over too great a range of activities or in too broad a geographic area, it shall be interpreted to extend only over the maximum period of time, range or activities or geographic area as to which it may be enforceable. If you violate the non-competition provisions set forth in this paragraph, you shall continue to be bound by such restrictions until a period of one (1) year has expired without any violation of such provisions.

4. **Disclosures** –

a. **Non-Disparagement** – Except as otherwise permitted by paragraph 4(c) below, this Agreement, and/or applicable law, you agree not to, in public or private, make any false, disparaging, derogatory or defamatory statements, online (including, without limitation, on any social media, networking, or employer review site) or otherwise, to any person or entity, including, but not limited to, any media outlet, industry group, financial institution or current or former employee, board member, consultant, client, or customer of the Company, regarding the Company or any of the other Released Parties, or regarding the business affairs, business prospects, or financial condition of the Company or any of the other Released Parties. Likewise, the Company agrees, through its senior executive officers and Board of Directors, not to, in public or private, make any false, disparaging, derogatory or defamatory statements, online (including, without limitation, on any social media, networking, or employer review site) or otherwise, to any person or entity, including, but not limited to, any media outlet, industry group, financial institution or current or former employee, board member, consultant, client, or customer of the Company, about you or your reputation. Notwithstanding the foregoing, nothing shall prohibit either party from making any statements (i) as required by law, and/or (ii) in order to enforce or defend against claims that are not released by this Agreement and asserted by you, on the one hand, against the Company and/or Released Party(ies), on the other hand, or vice versa. Further, you shall not be prohibited from making statements in the course of normal business competition as long as, in making such statement, you do not disparage the Company and do not otherwise violate the Restrictive Covenants Agreement.

b. **Confidentiality** – Except as otherwise permitted by paragraph 4(c) below and applicable law, you agree to maintain as confidential and not to disclose the terms and contents of this letter agreement, and the contents of the negotiations and discussions resulting in this letter agreement. For avoidance of doubt, nothing shall prohibit you from disclosing the terms and contents of this letter agreement in order to enforce and/or defend against claims arising out of this letter agreement.

c. **Permitted Disclosures** – Nothing in this letter agreement or elsewhere prohibits you from (a) communicating with government agencies about possible violations of federal, state, or local laws or otherwise providing information to government agencies, filing a complaint with government agencies, or participating in government agency investigations or proceedings, or (b) making disclosures or communications to engage in protected, concerted activity or to otherwise exercise rights under Section 7 of the National Labor Relations Act. You are not required to notify the Company of any such communications; provided, however, that nothing herein authorizes the disclosure of information you obtained through a communication that was subject to the attorney-client privilege. Further, notwithstanding your confidentiality and nondisclosure obligations, you are hereby advised as follows pursuant to the Defend Trade Secrets Act: “An individual shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of a trade secret that (A) is made (i) in confidence to a Federal, State, or local government official, either directly or indirectly, or to an attorney; and (ii) solely for the purpose of reporting or investigating a suspected violation of law; or (B) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal. An individual who files a lawsuit for retaliation by an employer for reporting a suspected violation of law may disclose the trade secret to the attorney of the individual and use the trade secret information in the court proceeding, if the individual (A) files any document containing the trade secret under seal; and (B) does not disclose the trade secret, except pursuant to court order."

5. **Company Affiliation** – You agree that, following the Separation Date, you will not hold yourself out as an officer, employee, or otherwise as a representative of the Company, and you agree to take reasonable steps to update any directory information that indicates you are currently affiliated with the Company. Without limiting the foregoing, you confirm that, within five (5) business days following the Separation Date, you will update any and all social media accounts (including, without limitation, LinkedIn, Facebook, Twitter and Four Square) to reflect that you are no longer employed by or associated with the Company.

6. **Return of Company Property** – You confirm that you have returned to the Company all keys, files, records (and copies thereof), equipment (including, but not limited to, computer hardware, software, printers, flash drives and other storage devices, wireless handheld devices, cellular phones, tablets, etc.), Company identification, and any other Company owned property in your possession or control, and that you have left intact, and have otherwise not destroyed, deleted, or made inaccessible to the Company, all electronic Company documents, including, but not limited to, those that you developed or helped to develop during your employment, and that you have not (a) retained any copies in any form or media; (b) maintained access to any copies in any form, media, or location; (c) stored any copies in any physical or electronic locations that are not readily accessible or not known to the Company or that remain accessible to you; or (d) sent, given, or made accessible any copies to any persons or entities that the Company has not authorized to receive such electronic or hard copies. You further confirm that you have cancelled all accounts for your benefit, if any, in the Company's name, including but not limited to, credit cards, telephone charge cards, cellular phone accounts, and computer accounts. Notwithstanding anything to the contrary in this letter agreement, you may retain your contact lists, whether in electronic or paper form (e.g., rolodex, Outlook contacts and calendar, etc.), and copies of documents related to your compensation and benefits, including the Employment Agreement, the 2021 Stock Incentive Plan, and any equity awards or grants.

7. **Business Expenses and Final Compensation** – You acknowledge that you have submitted requests for reimbursements by the Company for all business expenses incurred in conjunction with the performance of your employment and that, as of your Separation Date, except as previously submitted, no other reimbursements are owed to you. You further acknowledge that, as of the date of your separation of employment, you have received payment in full for all services rendered in conjunction with your employment by the Company, including payment for all wages, bonuses, and accrued, unused vacation time, and that no other compensation, benefit or consideration is owed to you except as provided , in this Agreement.

8. **Cooperation** – You agree that, to the extent permitted by law, you shall reasonably cooperate with the Company in the investigation, defense or prosecution of any claims or actions which already have been brought, are currently pending, or which may be brought in the future against the Company by a third party or by or on behalf of the Company against any third party, whether before a state or federal court, any state or federal government agency, or a mediator or arbitrator, of which you have knowledge as a result of your employment with the Company. Your reasonable cooperation in connection with such claims or actions shall include, but not be limited to, being reasonably available to meet with the Company's counsel, at reasonable times and locations designated by the Company, to investigate or prepare the Company's claims or defenses, to prepare for trial or discovery or an administrative hearing, mediation, arbitration or other proceeding and to act as a witness when requested by the Company. You further agree that, to the extent permitted by law, you will notify the Company promptly in the event that you are served with a subpoena (other than a subpoena issued by a government agency) or in the event that you are asked to provide a third party (other than a government agency) with information concerning any actual or potential complaint or claim against the Company.

9. **Amendment and Waiver** – This letter agreement shall be binding upon the parties and may not be modified in any manner, except by an instrument in writing of concurrent or subsequent date signed by duly authorized representatives of the parties hereto. This letter agreement is binding upon and shall inure to the benefit of the parties and their respective agents, assigns, heirs, executors, successors and administrators. No delay or omission by either party in exercising any right under this letter agreement shall operate as a waiver of that or any other right. A waiver or consent given by either party on any one occasion shall be effective only in that instance and shall not be construed as a bar to or waiver of any right on any other occasion.

10. **Validity** – Should any provision of this letter agreement be declared or be determined by any court of competent jurisdiction to be illegal or invalid, the validity of the remaining parts, terms or provisions shall not be affected thereby and said illegal or invalid part, term or provision shall be deemed not to be a part of this letter agreement.

11. **Nature of Agreement** – You understand and agree that this letter agreement is a severance agreement and does not constitute an admission of liability or wrongdoing on the part of the Company.

12. **Acknowledgments**[4] – You acknowledge that you have been given [a reasonable amount of time][at least twenty-one (21)/forty-five (45) days] to consider this letter agreement, and that the Company is hereby advising you to consult with an attorney of your own choosing prior to signing this letter agreement. You understand that you may revoke this letter agreement for a period of seven (7) business days after you sign this letter agreement by notifying me in writing, and the letter agreement shall not be effective or enforceable until the expiration of this seven (7) business day revocation period. [You understand and agree that by entering into this letter agreement, you are waiving any and all rights or claims you might have under the Age Discrimination in

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[4] Note: Bracketed text depends on age at time of termination.

Employment Act, as amended by the Older Workers Benefit Protection Act, and that you have received consideration beyond that to which you were previously entitled.]

13. **Eligibility for Severance Program**[5] – Attached to this letter agreement as Attachment A is a description of (i) any class, unit or group of individuals covered by the program of severance benefits which the Company has offered to you, and any applicable time limits regarding such severance benefit program; and (ii) the job titles and ages of all individuals eligible or selected for such severance benefit program, and the job titles and ages of all individuals in the same job classification or organizational unit who are not eligible or who were not selected for such severance benefit program.]

14. **Voluntary Assent** – You affirm that no other promises or agreements of any kind have been made to or with you by any person or entity whatsoever to cause you to sign this letter agreement, and that you fully understand the meaning and intent of this letter agreement. You further state and represent that you have carefully read this letter agreement, understand the contents herein, freely and voluntarily assent to all of the terms and conditions hereof, and sign your name of your own free act.

15. **Applicable Law; Equitable Remedies** – This letter agreement shall be interpreted and construed by the laws of the Commonwealth of Massachusetts, without regard to conflict of laws provisions. You hereby irrevocably submit to and acknowledge and recognize the jurisdiction of the courts of the Commonwealth of Massachusetts, or if appropriate, a federal court located in the Commonwealth of Massachusetts (which courts, for purposes of this letter agreement, are the only courts of competent jurisdiction), over any suit, action or other proceeding arising out of, under or in connection with this letter agreement or the subject matter hereof. Further, you acknowledge that the restrictions referenced and contained in Sections 3 and 4 of this letter agreement may be necessary for the protection of the business and goodwill of the Company and are considered by you to be reasonable for such purpose. You agree that any breach or threatened breach of such provisions may cause the Company substantial and irrevocable damage which is difficult to measure. Therefore, in the event of any such breach or threatened breach, you agree that the Company, in addition to such other remedies that may be available, shall have the right to seek an injunction from a court restraining such a breach or threatened breach without posting a bond, and the right to seek specific performance of such provisions, and you hereby waive the adequacy of a remedy at law as a defense to such relief. You further hereby irrevocably waive any right to a trial by jury in any action, suit or other legal proceeding arising under or relating to any provision of this letter agreement..

16. **Entire Agreement** – This letter agreement contains and constitutes the entire understanding and agreement between the parties hereto with respect to your severance benefits and the settlement of claims against the Company and cancels all previous oral and written negotiations, agreements, and commitments in connection therewith, except as otherwise set forth herein and except for the surviving provisions of the Employment Agreement. .

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[5] Note: Inclusion of paragraph and referenced attachment depends on age at time of termination and whether termination involves a group of employees.

17. **Tax Acknowledgement** – In connection with the severance benefits provided to you pursuant to this letter agreement, the Company shall withhold and remit to the tax authorities the amounts required under applicable law, and you shall be responsible for all applicable taxes with respect to such severance benefits under applicable law. You acknowledge that you are not relying upon the advice or representation of the Company with respect to the tax treatment of any of the severance benefits.

If you have any questions about the matters covered in this letter agreement, please call me at [insert phone number].

Very truly yours,

By: ________________________________
[Insert Name]
[Insert Title]

I hereby agree to the terms and conditions set forth above. I have been given [at least twenty-one (21)/forty-five (45) days][6] to consider this letter agreement, and I have chosen to execute this on the date below. I intend that this letter agreement will become a binding agreement between me and the Company if I do not revoke my acceptance in seven (7) business days.

____________________________ ________________________
[Insert Employee Name] Date

To be returned in a timely manner as set forth on the first page of this letter agreement, but not to be signed before the close of business on your last day of employment.

[6] Note: The timing depends on your age at separation from employment, and whether the termination involves a group of employees.

Exhibit 21.1

Subsidiaries of Ocular Therapeutix, Inc.

	Jurisdiction of Incorporation or Organization
Ocular Therapeutix Europe B.V.	The Netherlands
Ocular Therapeutix Securities Corp.	The Commonwealth of Massachusetts

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (Nos. 333-230659 and 333-275373) and Form S-8 (Nos. 333-198240, 333-202886, 333-210059, 333-216622, 333-223513, 333-230126, 333-237115, 333-254143, 333-258642, 333-263091, 333-266648, 333-270297, 333-273770 and 333-277244) of Ocular Therapeutix, Inc. of our report dated March 11, 2024 relating to the financial statements, which appears in this Form 10-K for the year ended December 31, 2023.

/s/PricewaterhouseCoopers LLP
Boston, Massachusetts
March 11, 2024

CERTIFICATIONS

I, Antony Mattessich, certify that:

1. I have reviewed this Annual Report on Form 10-K of Ocular Therapeutix, 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: March 11, 2024

By: /s/ Antony Mattessich
Antony Mattessich
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Donald Notman, certify that:

1. I have reviewed this Annual Report on Form 10-K of Ocular Therapeutix, 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: March 11, 2024

By: /s/ Donald Notman
Donald Notman
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Ocular Therapeutix, Inc. (the "Company") for the period ended December 31, 2023 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Antony Mattessich, President and Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that to his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 11, 2024

By: /s/ Antony Mattessich
Antony Mattessich
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Ocular Therapeutix, Inc. (the "Company") for the period ended December 31, 2023 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Donald Notman, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that to his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 11, 2024

By: /s/ Donald Notman
Donald Notman
Chief Financial Officer
(Principal Financial and Accounting Officer)

OCULAR THERAPEUTIX, INC.

Compensation Recovery Policy

This Compensation Recovery Policy (this "**Policy**") is adopted by Ocular Therapeutix, Inc. (the "**Company**") in accordance with Nasdaq Listing Rule 5608 ("**Rule 5608**"). This Policy is effective as of October 2, 2023 (the "**Effective Date**").

1. Definitions

(a) **"Accounting Restatement"** means a requirement that the Company prepare an accounting restatement due to the material noncompliance of the Company with any financial reporting requirement under the U.S. federal securities laws, including any required accounting restatement to correct an error in previously issued financial statements that is material to the previously issued financial statements, or that would result in a material misstatement if the error were corrected in the current period or left uncorrected in the current period. Changes to the Company's financial statements that do not represent error corrections are not an Accounting Restatement, including: (A) retrospective application of a change in accounting principle; (B) retrospective revision to reportable segment information due to a change in the structure of the Company's internal organization; (C) retrospective reclassification due to a discontinued operation; (D) retrospective application of a change in reporting entity, such as from a reorganization of entities under common control; and (E) retrospective revision for stock splits, reverse stock splits, stock dividends or other changes in capital structure.

(b) **"Committee"** means the Compensation Committee of the Company's Board of Directors (the "Board").

(c) **"Covered Person"** means a person who served as an Executive Officer at any time during the performance period for the applicable Incentive-Based Compensation.

(d) **"Erroneously Awarded Compensation"** means the amount of Incentive-Based Compensation that was Received that exceeds the amount of Incentive-Based Compensation that otherwise would have been Received had the amount of Incentive-Based Compensation been determined based on the restated amounts, computed without regard to any taxes paid by the Covered Person or by the Company on the Covered Person's behalf. For Incentive-Based Compensation based on stock price or total shareholder return, where the amount of Erroneously Awarded Compensation is not subject to mathematical recalculation directly from the information in an Accounting Restatement, the amount of Erroneously Awarded Compensation will be based on a reasonable estimate by the Committee of the effect of the Accounting Restatement on the stock price or total shareholder return upon which the Incentive-Based Compensation was Received. The Company will maintain documentation of the determination of that reasonable estimate and provide such documentation to Nasdaq.

(e) **"Executive Officer"** means the Company's officers as defined in Rule 16a-1(f) under the Securities Exchange Act of 1934, as amended.

(f) **“Financial Reporting Measures”** means (A) measures that are determined and presented in accordance with the accounting principles used in preparing the Company’s financial statements, and any measures that are derived wholly or in part from such measures (whether or not such measures are presented within the Company’s financial statements or included in a filing made with the U.S. Securities and Exchange Commission), (B) stock price and (C) total shareholder return.

(g) **“Incentive-Based Compensation”** means any compensation that is granted, earned, or vested based wholly or in part upon the attainment of a Financial Reporting Measure.

(h) Incentive-Based Compensation is deemed to be **“Received”** in the Company’s fiscal period during which the Financial Reporting Measure specified in the applicable Incentive-Based Compensation award is attained, even if the payment or grant of the Incentive-Based Compensation occurs after the end of that period or is subject to additional time-based vesting requirements.

(i) **“Recovery Period”** means the three completed fiscal years immediately preceding the earlier of: (A) the date the Board, a committee of the Board, or the officer or officers of the Company authorized to take such action if Board action is not required, concludes, or reasonably should have concluded, that the Company is required to prepare an Accounting Restatement; or (B) the date a court, regulator, or other legally authorized body directs the Company to prepare an Accounting Restatement. In addition, if there is a change in the Company’s fiscal year end, the Recovery Period will also include any transition period to the extent required by Rule 5608.

2. Recovery of Erroneously Awarded Compensation

Subject to the terms of this Policy and the requirements of Rule 5608, if the Company is required to prepare an Accounting Restatement, the Company will attempt to recover, reasonably promptly from each Covered Person, any Erroneously Awarded Compensation that was Received by such Covered Person during the Recovery Period pursuant to Incentive-Based Compensation that is subject to this Policy.

3. Interpretation and Administration

(a) Role of the Committee. This Policy will be interpreted by the Committee in a manner that is consistent with Rule 5608 and any other applicable law and will otherwise be interpreted in the business judgment of the Committee. All decisions and interpretations of the Committee will be final and binding.

(b) Compensation Not Subject to this Policy. This Policy does not apply to Incentive-Based Compensation that was Received before the Effective Date. With respect to any Covered Person, this Policy does not apply to Incentive-Based Compensation that was Received by such Covered Person before beginning service as an Executive Officer.

(c) Determination of Means of Recovery. Subject to the requirement that recovery be made reasonably promptly, the Committee will determine the appropriate means of recovery, which may vary between Covered Persons or based on the nature of the applicable Incentive-Based

Compensation, and which may involve, without limitation, establishing a deferred repayment plan or setting off against current or future compensation otherwise payable to the Covered Person. Recovery of Erroneously Awarded Compensation will be made without regard to income taxes paid by the Covered Person or by the Company on the Covered Person's behalf in connection with such Erroneously Awarded Compensation.

(d) Determination That Recovery is Impracticable. The Company is not required to recover Erroneously Awarded Compensation if a determination is made by the Committee that either (A) after the Company has made and documented a reasonable attempt to recover such Erroneously Awarded Compensation, the direct expense paid to a third party to assist in enforcing this Policy would exceed the amount to be recovered or (B) recovery of such Erroneously Awarded Compensation would likely cause an otherwise tax-qualified retirement plan, under which benefits are broadly available to employees of the registrant, to fail to meet the requirements of Section 401(a)(13) or 411(a) of the Internal Revenue Code and regulations thereunder.

(e) No Indemnification or Company-Paid Insurance. The Company will not indemnify any Covered Person against the loss of Erroneously Awarded Compensation and will not pay or reimburse any Covered Person for the purchase of a third-party insurance policy to fund potential recovery obligations.

(f) Interaction with Other Clawback Provisions. The Company will be deemed to have recovered Erroneously Awarded Compensation in accordance with this Policy to the extent the Company actually receives such amounts pursuant to any other Company policy, program or agreement, pursuant to Section 304 of the Sarbanes-Oxley Act or otherwise.

(g) No Limitation on Other Remedies. Nothing in this Policy will be deemed to limit the Company's right to terminate employment of any Covered Person, to seek recovery of other compensation paid to a Covered Person, or to pursue other rights or remedies available to the Company under applicable law.

Adopted by the Board on November 6, 2023.