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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, 2020
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	**20-5560161**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
24 Crosby Drive **Bedford, MA**	**01730**
(Address of principal executive offices)	**(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. ☐

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, 2020, the aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant was approximately $478 million. The number of shares outstanding of the registrant's class of common stock, as of March 1, 2021: 76,069,673.

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report incorporates by reference information from the definitive Proxy Statement for the registrant's 2021 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, 2020.

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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 and planned clinical trials, including our Phase 1 clinical trial of OTX-TIC for the reduction of intraocular pressure in patients with primary open-angle glaucoma or ocular hypertension, our Phase 1 clinical trial of OTX-TKI for the treatment of wet age-related macular degeneration, or wet AMD, our Phase 2 clinical trial of OTX-CSI for the chronic treatment of dry eye disease; and our Phase 2 clinical trial for OTX-DED for the short-term treatment of the signs and symptoms of dry eye disease;

- the preclinical and clinical development of our product candidate for the short-term treatment of the signs and symptoms of dry eye disease and our intravitreal implant with protein-based or small molecule drugs, including tyrosine kinase inhibitors, for the treatment of wet AMD, diabetic macular edema, or DME, and retinal vein occlusion, or RVO;

- our commercialization efforts for our product DEXTENZA®;

- our plans to develop, seek regulatory approval for and commercialize DEXTENZA for additional indications, including for the treatment of ocular itching associated with allergic conjunctivitis, for which we have been notified by the Food and Drug Administration of a target action date under the Prescription Drug User Fee Act of October 18, 2021, and our other product candidates based on our proprietary bioresorbable hydrogel technology platform;

- our ability to manufacture DEXTENZA, ReSure® Sealant and our product candidates in compliance with current Good Manufacturing Practices;

- our ability to manage a sales, marketing and distribution infrastructure to support the commercialization of DEXTENZA;

- the timing of and our ability to submit applications and obtain and maintain regulatory approvals for DEXTENZA, including the submission of a supplemental new drug application for the approval of the treatment of ocular itching associated with allergic conjunctivitis as an additional indication, and other product candidates;

- our estimates regarding expenses; future revenue; 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, ReSure Sealant, and our product candidates;

- the rate and degree of market acceptance and clinical utility of our products and our ability to secure and maintain reimbursement for our products;

- our estimates regarding the market opportunity for DEXTENZA, ReSure Sealant and our other product candidates;

- our strategic collaboration, option and license agreement with Regeneron Pharmaceuticals, Inc. under which we are collaborating on the development of an extended-delivery formulation of the vascular endothelial growth factor, trap aflibercept, currently marketed under the brand name Eylea, for the treatment of wet AMD, DME and RVO;

- our license agreement and collaboration with AffaMed Therapeutics Limited under which we are collaborating on the commercialization of DEXTENZA and our product candidate OTX-TIC in mainland China and certain other Asian countries;

- our capabilities and strategy, and the costs and timing of manufacturing, sales, marketing, distribution and other commercialization efforts, with respect to DEXTENZA, ReSure Sealant 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, including potential opportunities outside the field of ophthalmology;

- the impact of government laws and regulations;

- the costs and outcomes of legal actions and proceedings;

- uncertainty regarding the extent to which the COVID-19 pandemic and related response measures will adversely affect our business, results of operations and financial condition; 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 "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. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

SUMMARY OF RISKS RELATED TO OUR BUSINESS

Our business, financial condition, results of operations and future growth prospects 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. These risks include, but are not limited to, the following:

- We have incurred significant losses since our inception. Our net losses were $60.0 million for the year ended December 31, 2018, $86.4 million for the year ended December 31, 2019, and $155.6 million for the year ended December 31, 2020. As of December 31, 2020, we had an accumulated deficit of $539.3 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 may be forced to delay, reduce or eliminate our research and development programs or our commercialization efforts.

- 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 our obtaining marketing approval for and commercializing other products with significant market potential, including DEXTENZA for additional indications.

- DEXTENZA, ReSure Sealant 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. For example, DEXTENZA is currently scheduled to lose transitional pass-through status in July 2022. If pass-through status were to lapse, DEXTENZA would no longer be reimbursed separately from the ophthalmic surgery and our ability to generate revenues from the sales of DEXTENZA to ambulatory surgical centers and hospital out-patient departments for the treatment of post-surgical ocular inflammation and pain would be adversely affected.

- The COVID-19 pandemic has disrupted, and is expected to continue to adversely affect, our operations, including the progress of our commercialization of DEXTENZA and our ability to generate revenue from sales of DEXTENZA or ReSure Sealant. The COVID-19 pandemic may delay or adversely affect our clinical development activities, including our ability to recruit or retain patients in our ongoing clinical trials. We cannot be certain of the overall impact of COVID-19 on our business, financial condition and results of operations.

- Clinical trials of our product candidates may not be successful. We currently have several ongoing and planned clinical trials, including our Phase 1 clinical trial of OTX-TKI for the treatment of wet age-related macular degeneration, or wet AMD; our Phase 1 clinical trial of OTX-TIC for the reduction of intraocular pressure in patients with primary open-angle glaucoma or ocular hypertension; our Phase 2 clinical trial of OTX-CSI for the chronic treatment of dry eye disease; and our Phase 2 clinical trial for OTX-DED for the short-term treatment of the signs and symptoms of dry eye disease. If these or other 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 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 may not be successful in our efforts to develop products and product candidates based on our bioresorbable hydrogel technology platform, other than DEXTENZA and ReSure Sealant, or to expand the use of our bioresorbable hydrogel technology for treating additional diseases and conditions.

- We will depend heavily on our collaboration with Regeneron for the success of our extended-delivery hydrogel formulation in combination with Regeneron's large molecule VEGF-targeting compounds. If Regeneron does not exercise its option, terminates our collaboration agreement or is unable to meet its contractual obligations, it could negatively impact our business.

- If we are unable to establish and maintain adequate sales, marketing and distribution capabilities, scale up our manufacturing processes and 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, ReSure Sealant 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 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 product candidates, other than those developed under the Regeneron collaboration, 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.

PART I

Item 1. Business

Overview of Ocular Therapeutix

We are a biopharmaceutical company focused on the formulation, development and commercialization of innovative therapies for diseases and conditions of the eye using our proprietary, bioresorbable hydrogel platform technology. We use this technology to tailor duration and amount of delivery of a range of therapeutic agents in our product candidates.

We currently incorporate therapeutic agents that have previously received regulatory approval from the U.S. Food and Drug Administration, or FDA, including small molecules and proteins, into our hydrogel technology with the goal of providing local programmed-release of drug to the eye. We believe that our local programmed-release drug delivery technology has the potential to treat conditions and diseases of both the front and the back of the eye and can be administered through a range of different modalities including intravitreal implants, suprachoroidal implants, intracameral implants and intracanalicular inserts. We have product candidates in preclinical and clinical development designed to utilize this technology to treat retinal diseases including wet age-related macular degeneration, or wet AMD; glaucoma and ocular hypertension; and ocular surface diseases and conditions including dry eye disease and ocular itching associated with allergic conjunctivitis. We also have two FDA-approved products in commercialization in the United States: DEXTENZA®, an intracanalicular insert for the treatment of post-surgical ocular inflammation and pain, and ReSure® Sealant, an ophthalmic device designed to prevent wound leaks in corneal incisions following cataract surgery.

Our earlier-stage assets include four programs in clinical development:

- OTX-TKI, an axitinib intravitreal implant administered by fine-gauge needle for the treatment of wet AMD;
- OTX-TIC, a travoprost intracameral implant for the reduction of intraocular pressure, or IOP, in patients with glaucoma or ocular hypertension;
- OTX-CSI, a cyclosporine intracanalicular insert for the chronic treatment of dry eye disease; and
- OTX-DED, a dexamethasone intracanalicular insert for the short-term treatment of the signs and symptoms of dry eye disease.

We have a collaboration with Regeneron Pharmaceuticals, Inc., or Regeneron, for the development and potential commercialization of products containing our local programmed-release hydrogel in combination with Regeneron's vascular endothelial growth factor, or VEGF inhibitor, aflibercept, currently marketed under the brand name Eylea. We also continue to assess the potential use of our hydrogel platform technology in other areas of the body.

Retinal Disease Programs

We are engaged in the development of formulations of our hydrogel administered via intravitreal injection to address large markets for diseases and conditions of the back of the eye which we believe have significant growth potential. Our initial development efforts for our retinal disease programs have focused on the use of our extended-delivery hydrogel in combination with anti-angiogenic drugs, such as TKIs or protein-based anti-VEGF drugs, for the treatment of retinal diseases such as wet AMD; diabetic macular edema, or DME; and retinal vein occlusion, or RVO. Our initial goal for these programs is to provide extended delivery for at least six months, thereby reducing the frequency of the current monthly or bi-monthly immediate release intravitreal anti-VEGF injection regimens for wet AMD and other retinal diseases.

OTX-TKI (axitinib intravitreal implant)

Our product candidate OTX-TKI is a preformed, bioresorbable hydrogel fiber implant incorporating a small molecule tyrosine kinase inhibitor, or TKI, axitinib, with anti-angiogenic properties delivered by intravitreal injection

and designed for a duration of six months or longer. TKIs have shown promise in the treatment of wet AMD. In the first quarter of 2019, we began dosing patients in a multi-center, open-label, dose-escalation Phase 1 clinical trial in Australia designed to evaluate the safety, durability and tolerability of OTX-TKI. We are evaluating biological activity by measuring retinal thickness using spectral domain optical coherence tomography, or OCT, and following visual acuity over time. Two cohorts were initially enrolled: a lower dose cohort of 200 µg with six subjects and a higher dose cohort of 400 µg with seven subjects. We are actively enrolling a third cohort of 12 subjects, split between parallel arms of six subjects each. Subjects in the first arm of the third cohort will receive a dose of 600 µg, and subjects in the second arm will receive a 400 µg dose combined with an anti-VEGF induction injection.

At the Angiogenesis, Exudations, and Degeneration Virtual Conference in February 2021, we presented interim data from the Phase 1 clinical trial. In the Phase 1 clinical trial, OTX-TKI was observed to have a generally favorable safety profile, with no reported ocular serious adverse events. Some subjects in the Phase 1 clinical trial have shown a decrease in intraretinal or subretinal fluid by two months, and interim data suggests that OTX-TKI might have an extended duration of action beyond that of the current standard of care.

We plan to initiate a prospective, randomized, controlled Phase 1 clinical trial in the United States under an exploratory investigational new drug, or eIND, application in mid-2021 to evaluate a single implant 600 µg dose of OTX-TKI (combined with an anti-VEGF induction injection) in comparison with a 2 mg dose of aflibercept. We have requested a pre-investigational new drug, or IND, application meeting with the FDA to discuss the possibility of transitioning from an eIND application to a traditional IND application.

Pending our receipt and review of the topline data from the Phase 1 clinical trial in Australia and related regulatory discussions, we also plan to initiate a Phase 2 clinical trial in Australia to compare the administration of a single implant 600 µg dose of OTX-TKI (combined with an anti-VEGF induction injection) to a 2 mg dose of aflibercept dosed every 8 weeks as the comparator.

OTX-AFS (aflibercept suprachoroidal injection) in collaboration with Regeneron

As described above, in October 2016, we entered into a strategic collaboration, option and license agreement with Regeneron for the development and potential commercialization of products using our local programmed-release hydrogel in combination with, among other things, Regeneron's large molecule VEGF-targeting compounds for the treatment of retinal diseases, with the initial focus on the VEGF trap aflibercept. We and Regeneron amended this agreement in May 2020 to, among other things, transition joint efforts under the collaboration to the research and development of an extended-delivery formulation of aflibercept to be delivered to the suprachoroidal space which we refer to as OTX-AFS. Under the amended agreement, we have provided certain formulations to Regeneron who have agreed to perform preclinical assessments of OTX-AFS.

Glaucoma Program

Our development efforts for our glaucoma program have focused on the use of our extended-delivery hydrogel in combination with travoprost, an FDA-approved prostaglandin analog designed to lower elevated IOP. Our initial goal for this program is to provide extended delivery over at least four months with a single treatment.

OTX-TIC (travoprost intracameral implant)

Our product candidate OTX-TIC is a bioresorbable hydrogel implant incorporating travoprost 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. We are currently conducting a multi-center, open-label, dose-escalation, proof-of-concept Phase 1 clinical trial to evaluate the safety, biological activity, durability and tolerability of OTX-TIC compared to topical travoprost (eye drops) in patients with primary open-angle glaucoma or ocular hypertension. The trial consists of four patient cohorts: cohort 1 is 5 subjects who are receiving a 15 µg dose, cohort 2 is 4 subjects who are receiving a 26 µg dose, cohort 3 is 5 subjects who are receiving a 15 µg with a fast-degrading implant, and cohort 4 is 5 subjects who are receiving a 5 µg with a fast-degrading implant.

We presented interim data on all four patient cohorts at the Glaucoma360 Virtual Conference in January 2021. In this Phase 1 clinical trial, with a single implant, several subjects were able to achieve a decrease in IOP at least as large as that of the current standard of care. Many subjects exhibited an IOP-lowering effect of more than six months in

cohorts 1 and 2 and between three and six months in cohorts 3 and 4, the cohorts in which the fast-degrading implant was used. In the clinical trial, OTX-TIC was observed to have a generally favorable safety profile, with no reported ocular serious adverse events. Corneal health, as measured by endothelial cell counts, pachymetry assessments and slit lamp examinations did not indicate a clinically meaningful change from baseline.

In mid-2021, we plan to initiate a Phase 2 clinical trial to evaluate two formulations of OTX-TIC for the treatment of glaucoma or ocular hypertension in patients compared to Durysta (Allergan). The non-study eye of each patient will receive a topical prostaglandin daily. Certain subjects in the Phase 2 clinical trial will receive the same formulation used in cohort 1 of the Phase 1 clinical trial, containing a 26 µg dose of drug and utilizing a standard implant, and others will receive 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.

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 initial development efforts are focused on the use of our extended-delivery hydrogel in combination with well-known and well-understood drugs (cyclosporine and corticosteroids) for the treatment of dry eye disease and allergic conjunctivitis.

Dry Eye Disease

OTX-CSI (cyclosporine intracanalicular insert)

Our product candidate, 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 a duration of three to four months for patients suffering from moderate to severe dry eye and to be administered by a physician as a bioresorbable intracanalicular insert.

In October 2020, we reported topline data from our five subject Phase 1 clinical trial evaluating OTX-CSI in the 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 generally well-tolerated, and there were no adverse events of stinging, irritation, blurred vision or tearing reported or observed.

In September 2020, we dosed the first patients in a Phase 2 clinical trial designed to assess the safety, tolerability, and durability and to evaluate the efficacy of OTX-CSI for the chronic treatment of dry eye disease. The Phase 2 clinical trial is a U.S.-based, randomized, double-masked, multi-center trial evaluating two different formulations of OTX-CSI compared to a vehicle insert in approximately 140 subjects who are to be followed for a period of approximately 16 weeks. Endpoints include tear production as measured by the Schirmer's test; signs of dry eye disease as measured by corneal fluorescein staining; and symptoms of dry eye disease as measured by the visual analog scale, or VAS, eye dryness severity score and the VAS dry eye frequency score. We currently anticipate receiving topline data from this Phase 2 clinical trial by year-end 2021.

OTX-DED (dexamethasone intracanalicular insert)

Our product candidate 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 it includes a lower dose of the drug, delivers it via a smaller insert, and is designed to release it over a period of two to three weeks, compared with up to thirty days in the case of DEXTENZA. We believe that OTX-DED will address several of the current limitations of existing dry eye disease steroid treatments, the toxicity associated with preservatives, and the potential for abuse of topical steroids.

In February 2021, we dosed the first patient in a U.S.-based prospective, randomized, double-masked, vehicle-controlled Phase 2 clinical trial evaluating two different formulations of OTX-DED for the short-term treatment of the signs and symptoms of dry eye disease compared to a hydrogel insert in approximately 150 subjects. We anticipate receiving topline data from this Phase 2 clinical trial in the first half of 2022.

Allergic Conjunctivitis

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

DEXTENZA, incorporating the corticosteroid dexamethasone, is our FDA-approved intracanalicular insert for the treatment of post-surgical ocular inflammation and pain. We believe that allergic conjunctivitis represents a discrete potential market for DEXTENZA as a physician administered, hands-free, therapy administered in the office setting and designed to release preservative-free dexamethasone to the ocular surface for up to 30 days.

In April 2020, we reported topline results of a 96-subject, third pivotal Phase 3 clinical trial evaluating DEXTENZA for the treatment of ocular itching associated with allergic conjunctivitis. DEXTENZA-treated subjects demonstrated a statistically significant (p-value < 0.0001) difference in mean ocular itching scores, compared to vehicle-treated subjects, at all three pre-specified time points.

In the fourth quarter of 2020, we filed a supplemental new drug application, or sNDA, for DEXTENZA to include the treatment of ocular itching associated with allergic conjunctivitis as an additional indication. The FDA has accepted our sNDA for filing and has established a target action date under the Prescription Drug User Fee Act, commonly known as PDUFA, of October 18, 2021. If our sNDA is approved, we expect to launch DEXTENZA for the treatment of ocular itching associated with allergic conjunctivitis in the first half of 2022.

Post-Surgical Ocular Inflammation and Pain

DEXTENZA (dexamethasone ophthalmic insert) 0.4 mg for intracanalicular use for the Treatment of Post-Surgical Ocular Inflammation and Pain

As described above, DEXTENZA incorporates the FDA-approved corticosteroid dexamethasone as a preservative-free active pharmaceutical ingredient into a hydrogel, drug-eluting intracanalicular insert for the treatment of post-surgical ocular inflammation and pain. We commercially launched DEXTENZA in the United States 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.

In September 2020, we announced that we had dosed the first patients in a Phase 3 clinical trial evaluating DEXTENZA for the treatment of post-surgical ocular inflammation and pain in children following cataract surgery. This planned 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.

Additionally, we have received proposals for, and plan to support, several investigator-initiated trials evaluating DEXTENZA in different clinical situations. To date, third-party clinical investigators have initiated over 25 trials to study the use of DEXTENZA in cataract surgery, other ophthalmic surgeries and other potential indications. Seven of the trials have completed enrollment, and the remaining trials are actively enrolling and treated patients are being followed.

ReSure Sealant

In 2014, we commercially launched ReSure Sealant in the United States as a device approved to prevent wound leaks in corneal incisions following cataract surgery. In the pivotal clinical trials that formed the basis for FDA approval, ReSure Sealant provided superior wound closure and a better safety profile than sutured closure.

The FDA required two post-approval studies as a condition for approval of our premarket approval, or PMA, application for ReSure Sealant. The FDA has confirmed that first post-approval study, identified as the Clinical PAS, has been completed. The second post-approval study, which we refer to as the Device Exposure Registry Study, was a retrospective analysis of the IRIS Registry, comparing endophthalmitis rates from sites that purchased ReSure Sealant versus those sites that did not. We completed the retrospective study in accordance with our agreement with the FDA and submitted the final study report for the Device Exposure Registry Study to the FDA in January 2021. We anticipate

that the FDA will review the report within 90 days of our submission and notify us as to whether our obligation to conduct the post-approval study has been satisfied.

While ReSure Sealant remains commercially available in the United States, commercial and sales support for this product are modest at this time. We have received only limited revenues from ReSure Sealant to date and anticipate only limited sales for 2021.

AffaMed License Agreement

In October 2020, we entered into a license agreement and collaboration with AffaMed Therapeutics Limited, or AffaMed, for the development and commercialization of DEXTENZA and OTX-TIC in mainland China, Hong Kong, Macau, and Taiwan; South Korea; and the ASEAN markets (Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, the Philippines, Singapore, Thailand and Vietnam). Under the terms of the agreement, we received an upfront payment of $12 million and are 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. 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 OTX-TIC for the reduction of elevated intraocular pressure in patients with primary open-angle glaucoma or ocular hypertension in specified Asian markets. We retain the right to develop and commercialize DEXTENZA and OTX-TIC in all other global markets.

Additional Potential Areas for Growth

We continue to leverage the potential of our hydrogel platform to explore areas for growth with our focus on formulating, developing and commercializing innovative therapies for diseases and conditions of the eye. In September 2018, we entered into a second amended and restated license agreement, or Second Amended Agreement, with Incept LLC, an intellectual property holding company, or Incept. The Second Amended Agreement expanded the scope of our intellectual property license to include 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.

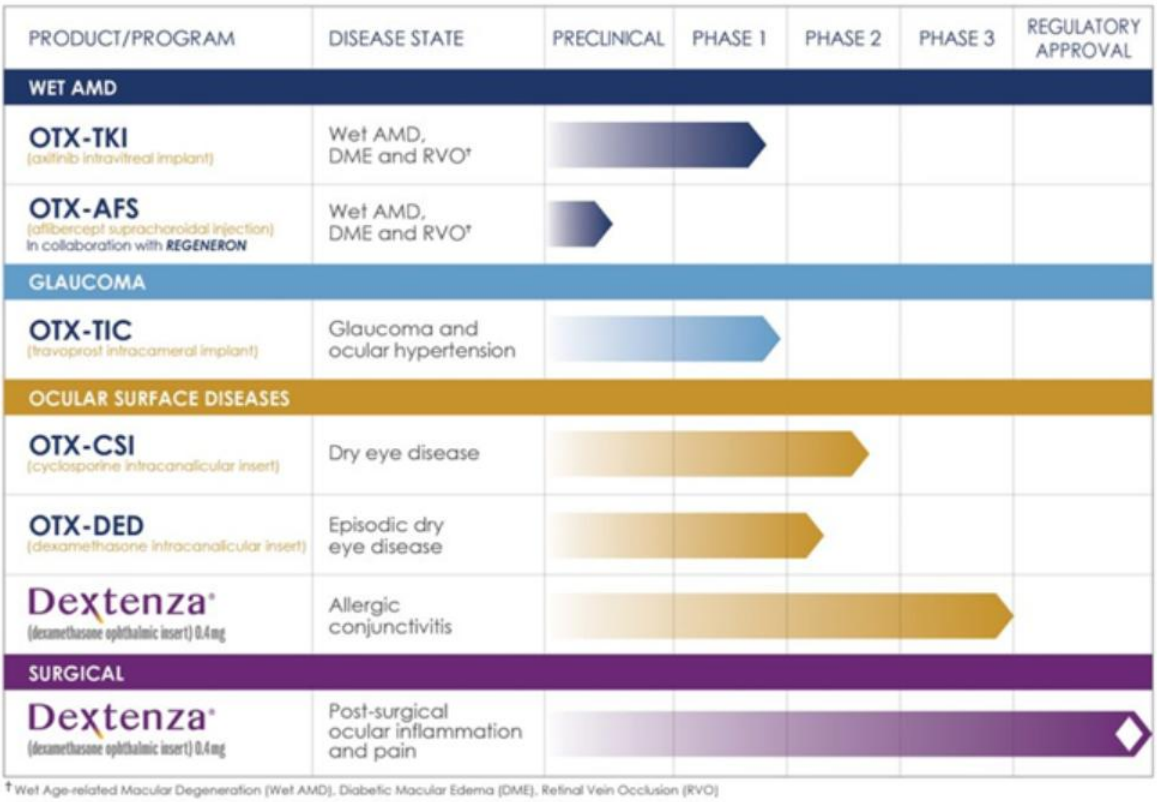
Market Background

Our clinical stage product candidates and our marketed products are based on a proprietary bioresorbable hydrogel technology platform that uses polyethylene glycol, or PEG, as a key component. Bioresorbable materials gradually break down in the body into non-toxic, water soluble compounds that are cleared by normal biological processes. PEG is used in many pharmaceutical products and is widely considered to be safe and biocompatible. Our technology platform allows us to tailor the physical properties, drug release profiles and bioresorption rates of our hydrogels to meet the needs of specific clinical indications. We have used this platform to engineer each of our intracanalicular insert, intracameral implant, and intravitreal implant product candidates; our suprachoroidal formulations; and ReSure Sealant. Our technical capabilities include a deep understanding of the polymer chemistry of PEG-based hydrogels and the design of the specialized manufacturing processes required to achieve a reliable, preservative-free and high purity product.

Product Pipeline

The following table summarizes the status of our key product development programs and DEXTENZA, our marketed product. We hold worldwide exclusive commercial rights to the core technology underlying all of our products in development and have not granted commercial rights to any marketing partners other than the option on commercial rights we granted to Regeneron for the delivery of protein-based anti-VEGF drugs in our hydrogel depot for the

treatment of retinal diseases and a license agreement and collaboration with AffaMed for the development and commercialization of DEXTENZA and OTX-TIC in the geographies agreed to between the parties.



Our Strategy

We are pursuing three overall strategic goals: to make prescription eye drops obsolete; to make immediate release back-of-the-eye injections obsolete; and to extend our hydrogel platform technology for use beyond the eye to other areas of the body. The key tactics of our strategy to achieve these goals are:

- *Advance our four core clinical development programs through Phase 2.* We believe the greatest potential value inflection points for us are the topline data readouts of the Phase 2 clinical trials of our four core clinical development programs: OTX-TKI for the treatment of wet AMD, OTX-TIC for the treatment of glaucoma or ocular hypertension, OTX-CSI for the treatment of dry eye disease, and OTX-DED for the short-term treatment of the signs and symptoms of dry eye disease.

- *Expand Commercialization of DEXTENZA for the treatment of ocular inflammation and pain following ophthalmic surgery.* We expect to grow our salesforce to increase our active number of accounts and penetrate each account more deeply. We intend to focus sales efforts on ambulatory surgical centers, or ASCs, that generate the largest volumes of cataract surgeries in the United States. We are also seeking to expand the label for DEXTENZA—beginning with our sNDA to add ocular itching associated with allergic conjunctivitis as an approved indication—to permit the product's use outside of the surgical setting and into ophthalmologists' offices.

- Apply our local programmed-release hydrogel-based technology to create additional proprietary solutions for ophthalmic diseases and conditions. In collaboration with Regeneron, we are conducting preclinical research

and development activities regarding an extended-delivery formulation of the VEGF trap aflibercept, currently marketed under the brand name Eylea, to be delivered to the suprachoroidal space. We are assessing preclinical product candidates for the ophthalmic space that leverage not only our proprietary PEG-based bioresorbable hydrogel technology platform but also active pharmaceutical ingredients used in FDA-approved ophthalmic drugs that are or are expected to become available on a generic basis. Finally, we are frequently in discussions with other companies operating in the ophthalmic space regarding potential collaborations to combine our local programmed-release hydrogel technology with their proprietary drug formulations to address additional diseases and conditions of the eye.

- *Address rest-of-world commercial opportunities through licensing and collaborations agreements*. In the fourth quarter of 2020, we announced a license agreement and collaboration with AffaMed for the development and commercialization of DEXTENZA and OTX-TIC in specified Asian markets. From time to time, we may consider additional arrangements with other companies to address markets outside of the United States.

- *Utilize our hydrogel platform to enable local programmed-release of therapeutics to areas of the body outside the eye.* We have licensed certain of Incept's intellectual property rights for the development of product candidates 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. We intend to explore programs outside of the eye not only on our own but also potentially through collaborations with third parties who have expertise and experience with other therapeutics as well as other areas of the body.

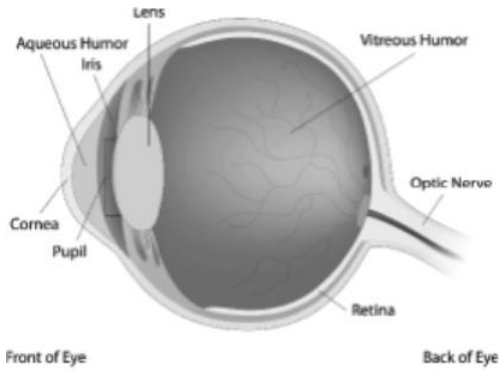
Eye Disease

Eye disease can be caused by many factors and can affect both the front and back of the eye.

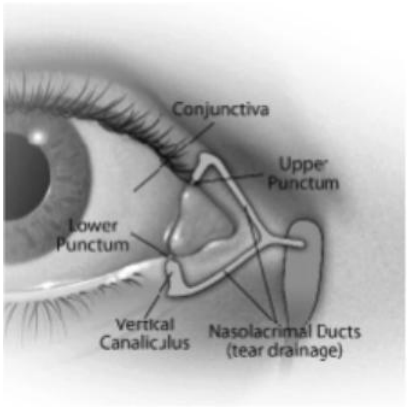
The front of the human eye consists of the cornea on the surface of the eye, the lens and the aqueous humor, which is a transparent fluid that fills the anterior chamber between the lens and the cornea. The tissue surrounding the eye also serves important functions. There is a natural opening, called a punctum, located in the inner portion of each upper and lower eyelid near the nose. The puncta open into nasolacrimal ducts, which collect and drain tears. The conjunctiva is the membrane covering the inside of the eyelids and the white part of the eye, known as the sclera. It helps to protect the eye from microbes and to lubricate the eye. Diseases and conditions affecting the front of the eye have generally been treated with either surgery or with medications delivered to the ocular surface by eye drops.

The back of the eye contains the retina, which is the light sensing layer of tissue; the vitreous humor, which is a transparent gel that fills the vitreous chamber between the lens and the retina; and the optic nerve, which transmits visual information from the retina to the brain. Eye disease can be caused by many factors and can affect both the front and back of the eye. Intravitreal injections or oral pills have typically been used to deliver medications to the back of the eye. Intravitreal injections or oral pills have typically been used to deliver medications to the back of the eye.

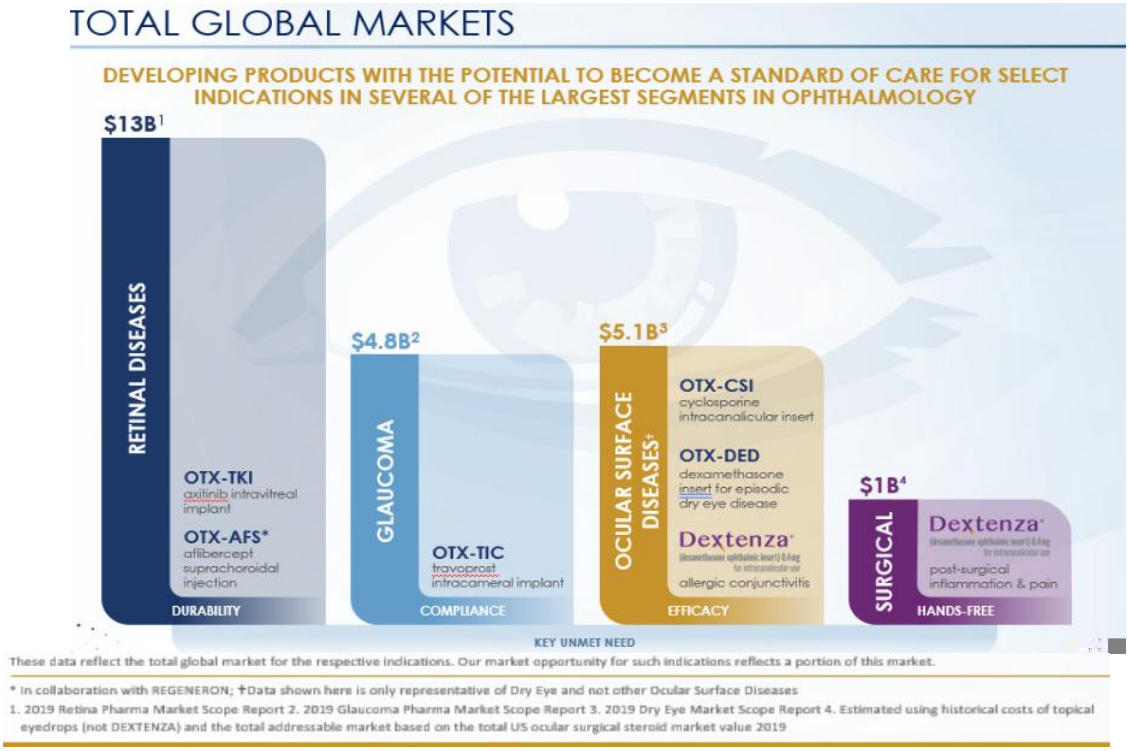
Cross Section of Eye



Tear Drainage System



We currently focus on some of the largest markets in ophthalmology. According to the Market Scope 2019 reports, our product candidates seek to address select indications within segments of ophthalmology that, in the aggregate, account for more than $20 billion global annual sales.



Retinal Diseases

One of the principal retinal diseases is wet AMD, a serious disease of the central portion of the retina, known as the macula, 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 leading cause of blindness in people over the age of 55 in the United States and the European Union. According to the 2019 Market Scope Retinal Disease Report, there are approximately 8.0 million people in the United States who suffer from vision-threatening retinal diseases. This population is expected to grow at a 2.4% compound annual growth rate through 2024.

Because eye drops are unable to carry effective drug concentrations to the back of the eye, intravitreal injections or oral medications are used to deliver medications to this location. However, the frequency of intravitreal injection can be a significant burden on patients, caregivers and clinicians. For example, the current treatment protocol for wet AMD involves monthly or bi-monthly injections. Intravitreal injections can lead to patient discomfort, a transient increase in IOP, and ocular inflammation and infection. Although serious adverse event rates after treatment with anti-VEGF compounds are low, intravitreal injections can result in severe complications and damage to the retina and other structures of the eye, such as ocular hemorrhage and tears in the retinal pigment epithelium.

Market Data

The global market for retinal disease was approximately $13.0 billion in 2019 and was estimated to grow at approximately 11% per year through 2024 according to Market Scope. The U.S. market accounted for just over 50% of the global market or $6.8 billion in 2019.

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 Beovu, marketed in the United States by Novartis. Avastin, a cancer treatment drug, marketed by Genentech, is also used off-label for the treatment of wet AMD.

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. Ocular hypertension is characterized by elevated levels of IOP without any optic nerve damage. Patients with ocular hypertension are at high risk of developing glaucoma.

Glaucoma impacts more than 2.7 million people age 40 or older in the United States. 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.

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.

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 products 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 $4.8 billion in 2019 with the U.S. market representing $1.9 billion.

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 Travatan Z (travoprost) marketed by Alcon and Lumigan (bimatoprost) marketed by Allergan. The relevant patents covering travoprost expired in December 2014. Commonly used generic drugs include latanoprost and timolol.

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 17.2 million patients diagnosed with dry eye disease in the United States, according to the Market Scope 2019 Dry Eye Products Market Report. Approximately 8.6 million of those patients are diagnosed with moderate to severe dry eye while the remaining 8.6 million patients are diagnosed with episodic 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 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 $5.1 billion in 2019 with the U.S. market representing $2.1 billion, composed of approximately $1.5 billion in prescriptions and $0.6 billion in over-the-counter medications. Within the prescription category, Restasis recorded sales in 2019 of approximately $1.2 billion in the United States while Xiidra recorded estimated sales of $0.3 billion in the United States.

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 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 IMS Health data, approximately 6.1 million anti-allergy eye drop prescriptions were filled in the United States in 2020, resulting in sales of approximately $401.2 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. 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. Pataday and Patanol formerly led the prescription market in this category but have recently been made available as over-the-counter products.

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 4.7 million ocular surgeries were to be performed in the United States in 2020, of which approximately 3.2 million are estimated to be cataract surgeries. In 2021, Market Scope estimates 5.1 million cataract surgeries are to be performed. We focus our sales efforts 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 $538.83 per insert, we estimate that there is a near-term addressable market of approximately $1 billion per year in the surgical space.

According to IMS Health data, approximately 17.7 million prescriptions were filled in the United States in 2020 for anti-inflammatory drugs administered by prescription eye drops for ocular diseases and conditions, resulting in sales of approximately $4.3 billion. These prescriptions consisted of approximately 7.4 million prescriptions and $580.0 million in sales for single-agent corticosteroids, 2.8 million prescriptions and $293.4 million in sales for NSAIDs, 3.7 million prescriptions and $262.7 million in sales for corticosteroid and antibiotic combination products and approximately 3.6 million prescriptions and $2.9 billion in sales of Restasis and Xiidra for dry eye disease.

The Use of Eye Drops and its Limitations

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. For example, steroids for ophthalmic use require administration as frequently as four to six times daily and require tapered dosing over the course of the therapy. As a result, patient compliance with required dosing regimens frequently suffers. According to a published third-party study, more than 50% of glaucoma patients are not compliant with their prostaglandin therapy and do not refill prescriptions as required or do not follow the prescribed regimen within six months of initiating therapy. Poor patient compliance can lead to diminished efficacy and disease progression.

- *Difficulty in administration*. Eye drops are difficult to administer for many patients, in particularly the elderly, due to physical or mental conditions such as arthritis or dementia. Difficulty in self-administering eye drops may lead to bacterial contamination in the bottle resulting from incorrect usage, limited accuracy administering the drops directly into the eye and the potential washout of drops from the eye. 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**.**

Challenges of 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, DME and RVO are among the most common conditions treated with intravitreal anti-VEGF 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. 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. And 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.

Ocular Wound Closure

According to the World Health Organization, cataracts are the leading cause of visual impairment eventually progressing to blindness. According to the American Academy of Ophthalmology Cataract and Anterior Segment Panel's 2011 Preferred Practice Pattern Guidelines, cataract extraction is the most commonly performed eye surgery in the United States. Market Scope has estimated that in 2019 there were approximately 4.0 million cataract extractions performed in the United States.

A cataract is a clouding of the lens inside the front of the eye. During cataract surgery, a patient's cloudy natural lens is removed and replaced with a prosthetic intraocular lens. Clear corneal incision that allows entry to the eye is the typical method for performing cataract surgery. The most common post-surgical approach is to allow the incisions to self-seal, or close, through normal biological processes. However, self-sealing incisions can open spontaneously, especially within 12 to 24 hours following surgery, when IOP fluctuates or as a result of the application of external pressure or manipulation. In addition, incisions that are left to self-seal may leak, which can sometimes result in complications. Complications from fluid leakage include the development of hypotony, or low IOP, which can lead to corneal decompensation and vision loss, as well as the potential for infection. The implanted intraocular lens also may shift in position due to hypotony, leading to reduced visual outcomes following surgery.

Sutures are the most widely used alternative method of wound closure. However, sutures do not completely prevent fluid leakage, are time-consuming to place and have been associated with patient discomfort, corneal distortion, and shallowing of the interior chamber. Sutures may also lead to astigmatism, a distortion of the cornea. An additional visit may be required to remove sutures, thus adding time, inconvenience and expense to the surgical process. These shortcomings limit the use of sutures in ophthalmic surgery. In a 2012 survey of ophthalmologists in the United States conducted by Lachman Consulting LLC, a healthcare consulting firm, respondents indicated that they use sutures in approximately 14% of cataract surgeries.

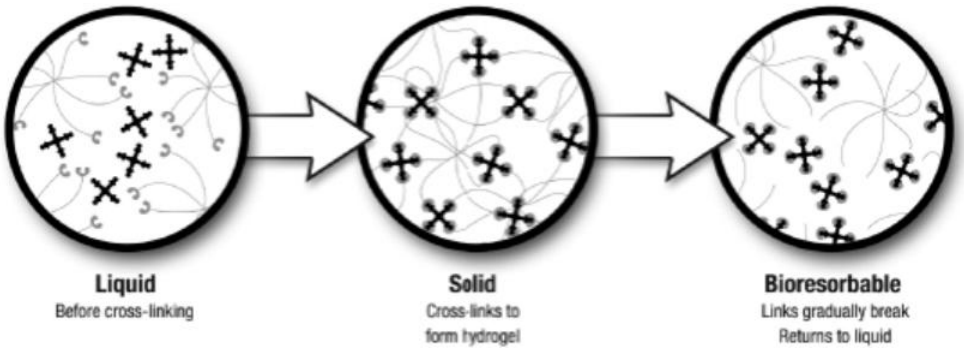
The Ocular Therapeutix Approach

Our Hydrogel Technology Platform

We apply our expertise with an established bioresorbable hydrogel technology 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.

Our bioresorbable hydrogel technology 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.

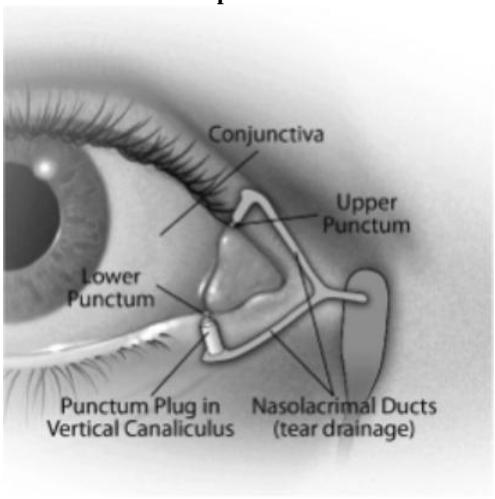
We create our hydrogels by cross-linking PEG molecules to form a network that resembles a three-dimensional mesh on a molecular level. Our PEG molecules are branched, with four to eight branches or arms. Each arm bears a reactive site on its end. Our cross-linking chemistry uses a second molecule with 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 several months. The figure below depicts the formation and bioresorption of the hydrogel for ReSure Sealant.



Intracanalicular Inserts

A punctum is a natural opening located in the inner portion of the eyelid near the nose. There is a punctum in each of the lower eyelids and the upper eyelids. The puncta open into nasolacrimal ducts, which collect and drain tears produced by the eyes' lacrimal glands. Tears produced in the lacrimal glands sweep across the eye surface and drain through the puncta to the nasal cavity. The section of the nasolacrimal duct immediately beyond the puncta is called the vertical canaliculus. Intracanalicular inserts that do not contain an active drug are commonly used for treatment of dry eye disease by physically blocking tear drainage. Because intracanalicular inserts stay in contact with the tear film, they are well suited for local programmed-release of drug to the eye.

Intracanalicular insert shown positioned in the vertical canaliculus

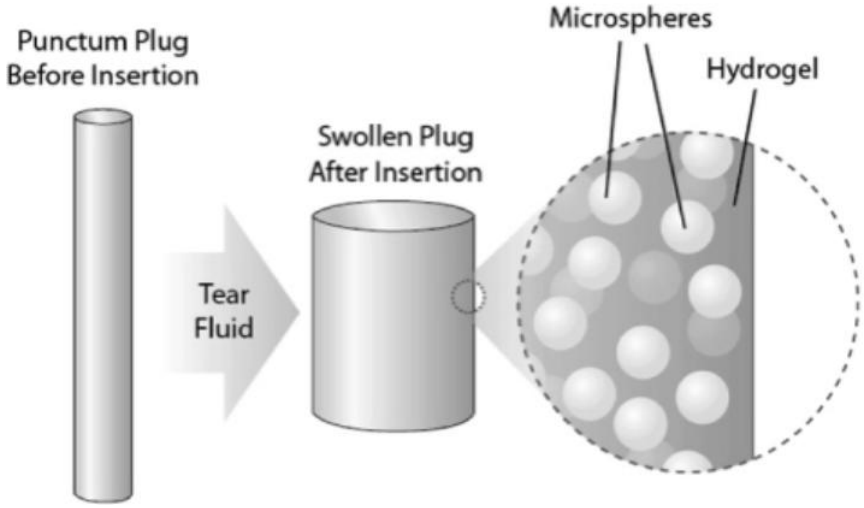


Our intracanalicular inserts utilize our proprietary hydrogel technology and are embedded with an active drug. Following insertion through the punctum, our inserts swell in tear fluid to fill the vertical canaliculus, which secures the inserts in place. We design our inserts to release drug in a programmed fashion, tailored to each disease state, back through the punctum to the surface of the eye. 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.

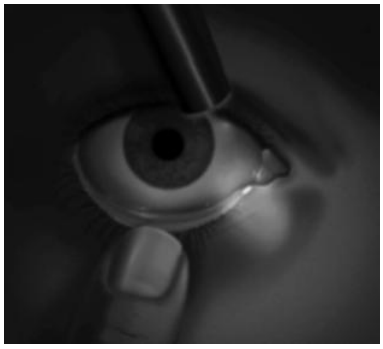
Our inserts allow incorporation of a variety of drugs with a controllable range of delivery durations and delivery rates. For acute conditions, such as post-surgical ocular inflammation and pain and ocular itching associated with allergic conjunctivitis, we have designed our intracanalicular inserts to provide a local programmed-release of therapeutic levels of drug for the duration of treatment. For chronic diseases, such as glaucoma, we have designed our intracanalicular inserts for repeat administration with extended dosing periods. We are concentrating our initial development efforts on intracanalicular inserts incorporating active pharmaceutical ingredients that are approved by the FDA for the targeted indication and that satisfy other specific selection criteria that we have developed.

We manufacture our intracanalicular inserts from dried PEG-based hydrogel formed into tiny rods that hold an active pharmaceutical ingredient in a preservative-free formulation. We embed the active pharmaceutical ingredient in the pre-hydrogel liquid formulation, which then solidifies to form a hydrogel containing the drug within. The relative size of one of our intracanalicular inserts is shown in the figure below.

We provide the intracanalicular insert as a thin dry rod to facilitate insertion through the narrow punctal opening. Upon hydration with tear fluid, the insert swells, softens, and conforms to roughly the size and shape of the vertical canaliculus, to secure it in place. We incorporate the active pharmaceutical ingredient in the form of micronized particles embedded directly in the hydrogel or as bioresorbable microspheres.



We have included a fluorescent label, or marker, in our intracanalicular insert hydrogel to serve as a visualization aid for the healthcare professional to confirm the insert's presence. The viewer applies a blue handheld light and a clear yellow filter aid to see the insert in the eyelid as shown in the figure below.



Because intracanalicular inserts stay in contact with the tear film, other companies have pursued the development of intracanalicular punctum plugs containing active drugs for local programmed release to the ocular surface. However, these earlier product designs had significant limitations with respect to drug capacity, drug release kinetics and patient comfort and used non-degradable punctum plugs with a clear silicone hard rubber shell containing only a core with active drug. These plugs typically extended outside of the punctal opening and secured themselves in place with an external cap. The external cap was in constant contact with the surface of the eye, which may cause irritation and discomfort in some cases. In addition, some prior designs resorted to plugging both the upper and lower puncta, which could cause excessive tearing and patient discomfort. These designs did not incorporate a visualization agent to allow the patient and physician to assess the presence of the plug.

In contrast to these prior approaches, we have designed our intracanalicular inserts to:

- incorporate the active pharmaceutical ingredient throughout the insert rather than just in a core to allow for higher drug capacity and better control over drug release;
- be bioresorbable so that removal is not required for acute conditions and required infrequently for chronic conditions;
- be soft and to fit beneath the punctal opening for patient comfort; and

- include a fluorescent label to allow the healthcare professional and patient to visualize and assess the presence of the insert.

We select the active pharmaceutical ingredients for our local programmed-release drug delivery product candidates, including our intracanalicular inserts, based on criteria we have developed through our extensive experience with hydrogel insert systems. Our active pharmaceutical ingredient selection criteria include:

- prior approval by the FDA for the targeted ophthalmic indication, except for our OTX-TKI 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;
- availability from a qualified supplier; and
- compatibility with our drug delivery system.

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

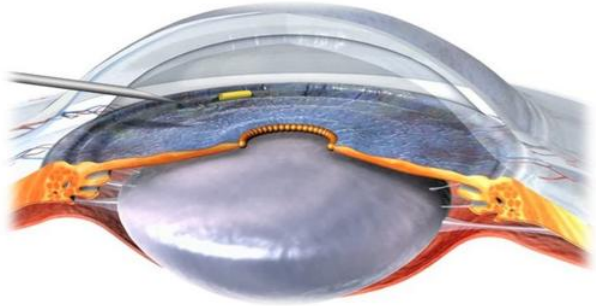
- *Improved patient compliance*. Our inserts and implants are placed by a healthcare professional and are designed to provide local programmed-release of drug to the ocular surface. Because patients are not responsible for self-administration of the drug and the inserts and implants dissipate over time 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 several months for chronic conditions. We believe this avoids the need for frequent administration and the 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. 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.

Intracameral Implants

We are engaged in the clinical development of our hydrogel administered via intracameral injection to address retinal diseases.

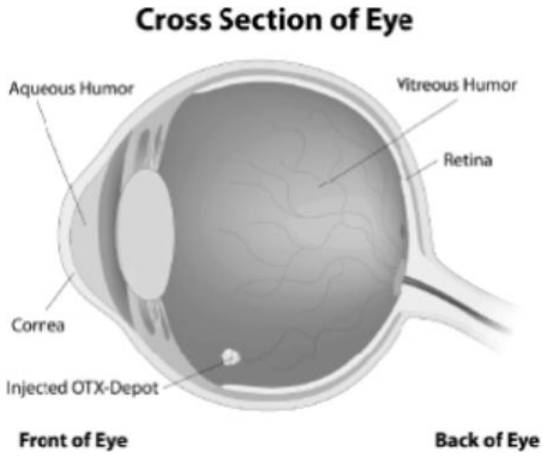
Intracameral implants refer to biodegradable or bioresorbable implants placed into the anterior chamber or front of the eye for the treatment of ocular conditions. The implants are designed to be held in place by currents and gravity present in the anterior chamber of an eye. As an example, in the case of OTX-TIC, 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 consist of a PEG-based hydrogel suspension, which contains embedded micronized particles of active drug. We designed the intravitreal implant to be injected and retained in the vitreous humor, as depicted in the figure below, to provide local programmed-release intravitreal delivery of anti-VEGF compounds.



Our initial intravitreal implant development efforts are focused on the use of our programmed-release hydrogel in combination with anti-angiogenic compounds such as protein-based anti-VEGF drugs or small molecule drugs, such as TKIs, for the treatment of retinal diseases, including wet AMD, RVO and DME. Our initial goal for these programs is to provide extended delivery of a protein-based large molecule or small molecule TKI targeting VEGF and other indications over a six-month period or longer following administration of a bioresorbable hydrogel incorporating the drug by an injection into the vitreous humor. This approach would reduce the frequency of the current monthly or bi-monthly intravitreal injection regimen for wet AMD and other retinal diseases and potentially provide a more consistent, uniform release of drug over the treatment period.

We believe TKIs are well suited for use with our platform given their high potency, multi-target capability, and compatibility with a hydrogel vehicle. In the absence of a sophisticated drug delivery system, these drugs have been difficult to deliver to the eye for acceptable timeframes at therapeutic levels without causing local and systemic toxicity due to low drug solubility and notably short half-lives in solution. We believe our local drug delivery technology gives us potential advantages in this regard.

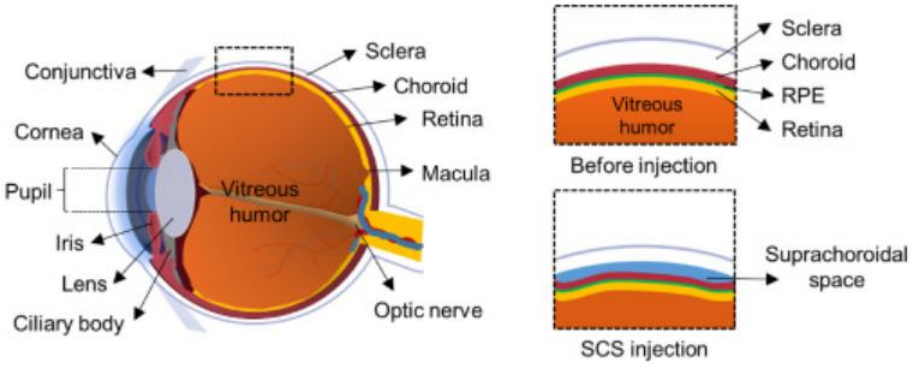
We have designed our intravitreal implant for delivery using typically available syringes and fine gauge needles compatible with the current standard of care. Once in the vitreous humor, the hydrogel is designed to retain properties of

TKI and anti-VEGF compounds until they are released. We have designed the hydrogel to liquefy, dissolve and be cleared from the eye through hydrolysis over time. We design our hydrogels to control the hydrogel biodegradation rate and, as a result, the timing of TKI and anti-VEGF compound release.

By selecting a compound that is compatible with our hydrogel platform technology and that will have expiration of relevant patents within the timeline of our development program, we avoid the need to license the TKI molecule, thus retaining full worldwide rights to any products we develop.

Suprachoroidal Injections

The suprachoroidal space, which we refer to as the SCS, is a potential space between the sclera and choroid that traverses the circumference of the posterior segment of the eye. The SCS is believed to be an attractive site for drug delivery because drugs are able to target the choroid, retinal pigment endothelium and retina with high bioavailability while maintaining low levels of drug elsewhere in the eye.



ReSure Sealant for Ocular Wound Closure

ReSure Sealant is our bioresorbable hydrogel device for wound closure following cataract surgery. A surgeon applies ReSure Sealant as a liquid painted onto the corneal incision. Within about 15 seconds, the sealant cross-links and transforms into a smooth, lubricious hydrogel that seals the wound. ReSure Sealant dissipates as healing progresses and does not require removal. In the pivotal clinical trials that formed the basis for FDA approval, ReSure Sealant provided superior wound closure and a better safety profile than sutured closure.

Development Pipeline and Marketed Products

The following table summarizes important information about our key product development programs and our marketed products, DEXTENZA and ReSure Sealant. We hold worldwide commercial rights to each of our product candidates, DEXTENZA and ReSure Sealant.

Product / Program	Indication	Description (Active Pharmaceutical Ingredient)	Stage of Development	Status
Preclinical Stage Product Candidates				
OTX-AFS	Wet AMD, DME and RVO	Suprachoroidal implant (Aflibercept)	Preclinical	In collaboration with corporate partner Regeneron.
Early-Stage Clinical Product Candidates				
OTX-TKI	Wet AMD	Intravitreal implant (Axitinib)	Phase 1	Australian Phase 1 clinical trial ongoing. Plan to initiate Phase 1 trial in the United States under eIND in Q2 2021. Plan to initiate a Phase 2 clinical trial in Australia, pending the receipt and review of topline data from the Phase 1 clinical trial in Australia.
OTX-TIC	Glaucoma or ocular hypertension	Intracameral implant (Travoprost)	Phase 1	Phase 1 clinical trial ongoing. Plan to commence Phase 2 clinical trial mid-2021.
OTX-CSI	Treatment of dry eye disease	Intracanalicular insert (Cyclosporine)	Phase 2	Phase 2 clinical trial ongoing; topline data anticipated in Q4 2021.
OTX-DED	Short-term treatment of signs and symptoms of dry eye disease	Intracanalicular insert (Dexamethasone)	Phase 2	Commenced Phase 2 clinical trial in first quarter 2021; topline data anticipated in first half 2022.
Late Stage Clinical Product Candidates				
DEXTENZA	Allergic conjunctivitis	Intracanalicular insert (Dexamethasone)	sNDA filed	PDUFA target action date of October 18, 2021.
Approved Product				
DEXTENZA	Post-surgical ocular inflammation and pain	Intracanalicular insert (Dexamethasone)	Marketed	Product commercially launched in the United States in July 2019.
ReSure Sealant	Cataract incision closure	Ocular sealant	Marketed	Product commercially launched in the United States in February 2014.

Retinal Disease Programs

OTX-TKI (axitinib intravitreal implant)

Our current intravitreal implant development efforts are focused on the use of our sustained-release hydrogel in combination with anti-angiogenic compounds, including anti-VEGF compounds, for the treatment of wet AMD. Our

initial implants have delivered anti-VEGF compounds *in vitro* over our targeted four to six month period, which we believe could make it possible to reduce the frequency of the current monthly or bi-monthly intravitreal injection regimen for wet AMD. In addition, our preclinical studies demonstrated a sustained pharmacodynamic effect *in vivo* of over six months with a small molecule TKI.

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.

In Vitro and preclinical results

We have conducted *in vivo* pharmacokinetic and pharmacodynamic studies with hydrogels loaded with axitinib injected intravitreally. Pharmacokinetic data showed retinal tissue drug concentrations in excess of 3,000 times the published concentration needed to inhibit VEGF by 50% after six months and pharmacodynamic results show sustained efficacy for six months.

Phase 1 clinical development

We are conducting an open-label, proof-of-concept Phase 1 clinical trial of OTX-TKI for the treatment of patients with neovascular age related macular degeneration, or wet AMD, caused by excessive blood vessel growth in the back of the eye due to VEGF. OTX-TKI is a bioresorbable hydrogel implant incorporating axitinib that is designed to be delivered via intravitreal injection into the vitreous humor of the eye and has an initial target duration of drug release for approximately six to nine months. Preclinical studies to date have demonstrated suppression of vascular leakage and good pharmacokinetics in the relevant ocular tissues. The Phase 1 clinical trial was submitted to the Therapeutic Goods Administration, Australia's regulatory authority for therapeutic goods, in July 2018.

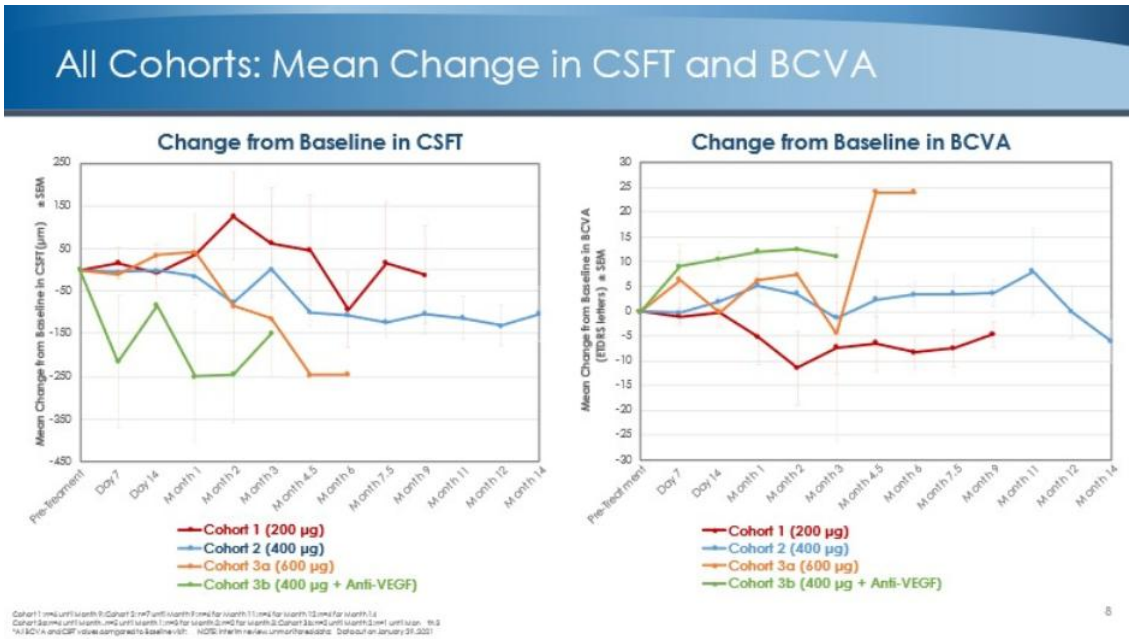
In the first quarter of 2019, we began dosing subjects in a Phase 1 clinical trial in Australia. This clinical trial is a prospective, multi-center, open-label, does escalation study designed to evaluate the safety, durability, tolerability, and biological activity of OTX-TKI. We are evaluating biological activity by following visual acuity over time and measuring retinal thickness using standard optical coherence tomography, or OCT. Two cohorts have been enrolled, a lower dose cohort of 200 µg of six subjects and a higher dose cohort of 400 µg of seven subjects. In the first two fully enrolled cohorts, OTX-TKI was generally well tolerated and observed to have a favorable safety profile with no ocular serious adverse events noted. In the higher dose cohort, OTX-TKI showed a decrease in central subfield retinal thickness as measured by mean change in central subfield thickness values by decreases in intraretinal and/or subretinal fluid in some subjects.

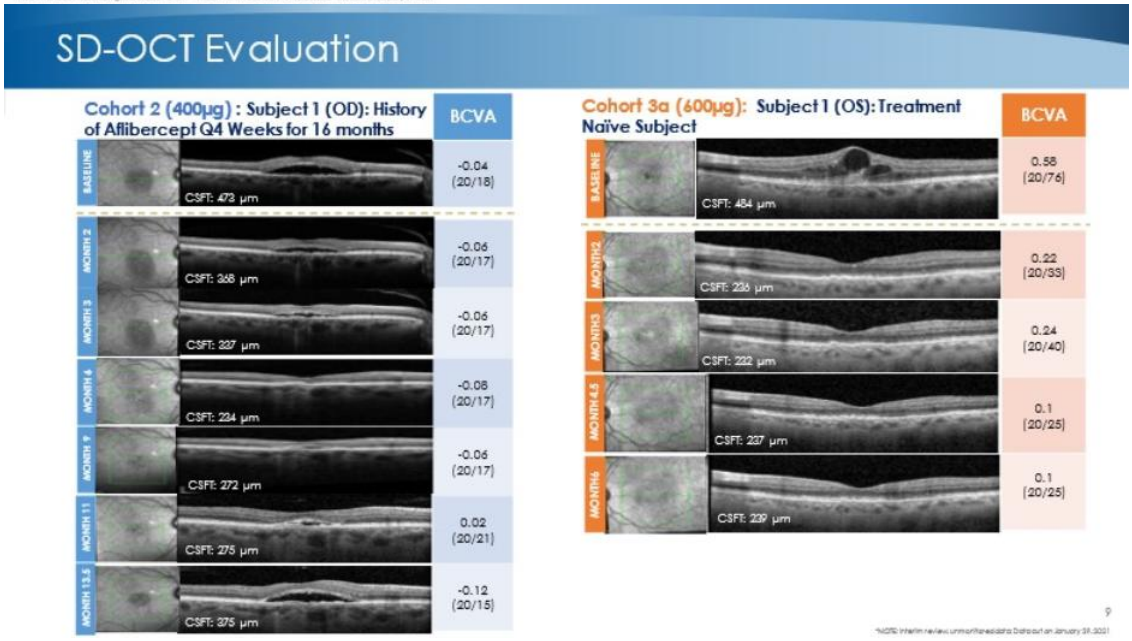
We amended our clinical trial protocol to enroll two additional cohorts, cohort 3a consisting of six patients being administered a 600 µg dose and cohort 3b consisting of six patients being administered a 400 µg dose plus an induction injection of the anti-VEGF drug aflibercept. Cohort 3a is fully enrolled and patients are being monitored while cohort 3b is still enrolling.

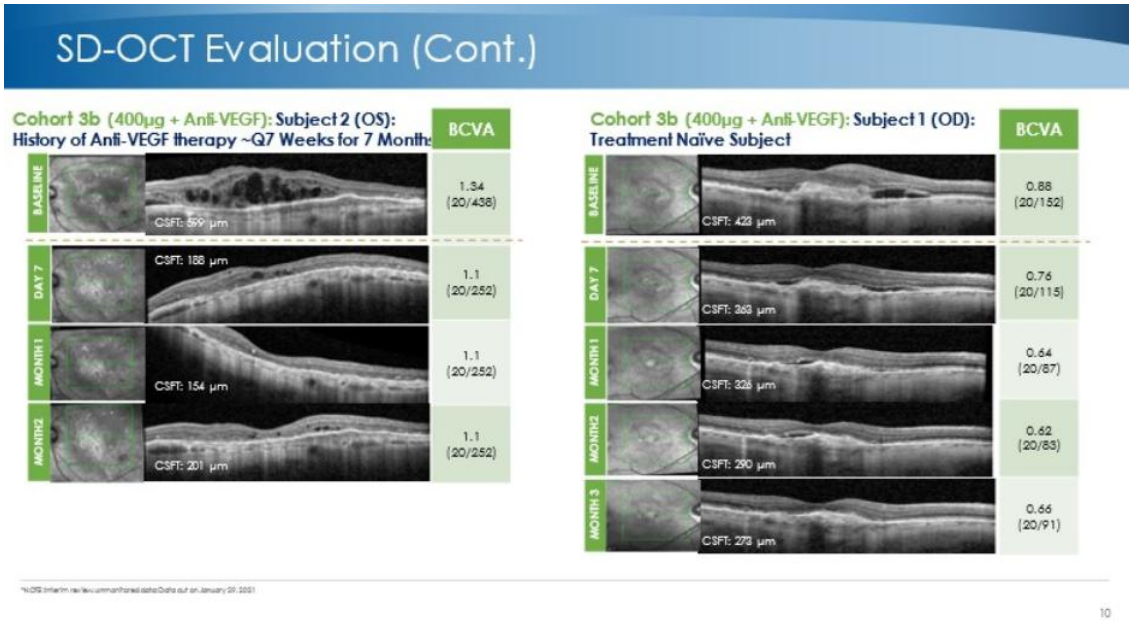
In February, interim data from this Phase 1 clinical trial of OTX-TKI was presented at the Angiogenesis, Exudation and Degeneration 2021 Virtual conference hosted by the Bascom Palmer Eye Institute, University of Miami Health System. We believe that OTX-TKI has demonstrated a preliminary signal of biological activity as observed by a clinically-meaningful decrease in retinal fluid as measured by high resolution OCT that provides cross-sectional images of the anatomical structure of the retina. As observed in cohort 2 (400 µg dose) and cohort 3a (600 µg dose), some subjects showed a decrease in intraretinal or subretinal fluid by two months after injection. In cohort 3b (400 µg dose plus anti-VEGF induction injection of aflibercept), two subjects were observed to have a decrease in intraretinal and/or subretinal fluid as early as a week after injection.

In addition, the OTX-TKI implants in cohort 1 were observed to have biodegraded in all subjects within 9 to 10.5 months of injection. It has also been observed that the implants are able to be adequately monitored and that there is limited to no movement of the implant in the anterior segment of the eye.

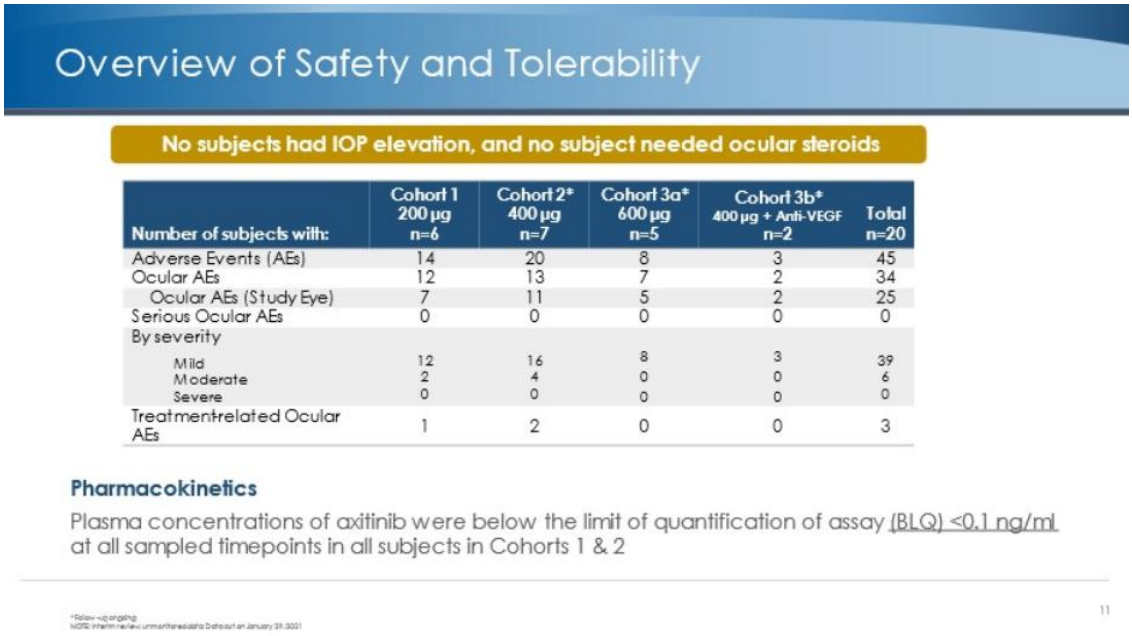
These findings are supported by the graphs below that present the mean change in central subfield thickness, or CSFT, and in best corrected visual acuity, or BCVA, across the four cohorts as well as specific patient images from cohorts 2, 3a and 3b showing declines in intraretinal and/or subretinal fluid over time.





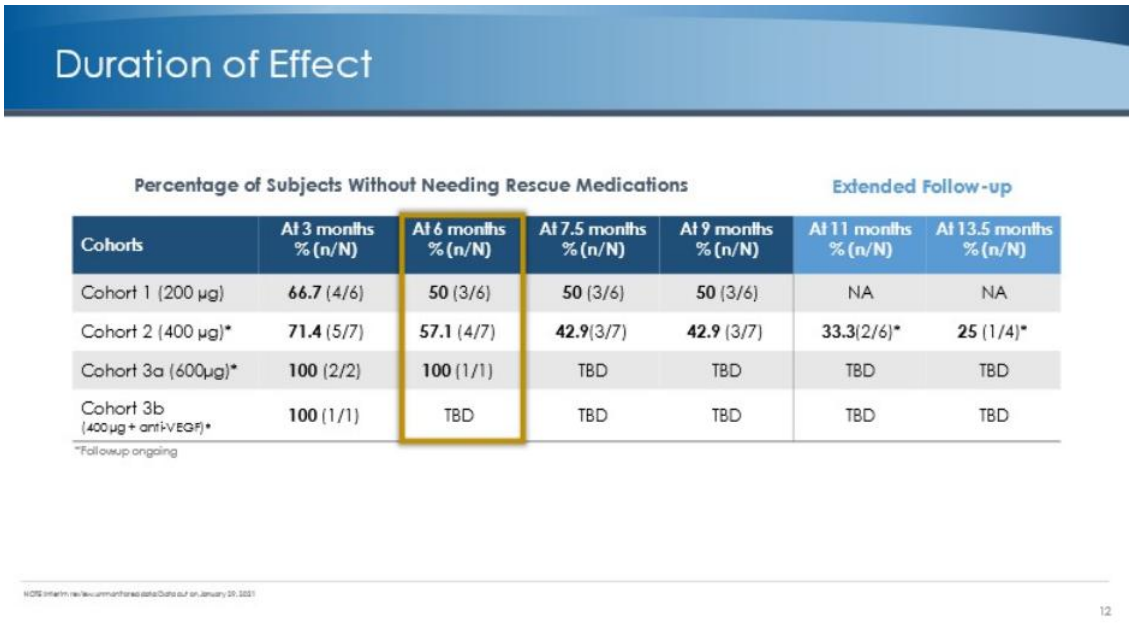


OTX-TKI has been observed to have a favorable safety profile and be generally well-tolerated to date. There have been no ocular serious adverse events reported. Plasma concentrations of the active drug (axitinib) were measured to be below the limit of quantification of assay, or BLQ < 0.1 ng/ml, at all sampled time points for all patients in cohorts 1 and 2. This assessment indicates that there is no measurable systemic exposure to axitinib.



We believe that the interim data suggests that OTX-TKI is durable and may extend the duration of action beyond several months. As noted in the table below, 50% of cohort 1 (200 µg dose) subjects, or 3 out of 6, and 57% of cohort 2 (400 µg dose) subjects, or 4 out of 7, did not require rescue medication at or before six months post-injection. Further, several subjects in cohort 2 demonstrated durability of therapy for over 6 months and one subject demonstrated

durability out to 13.5 months without rescue. In cohort 3a, one subject has demonstrated durability of therapy up to six months so far. Follow-up remains ongoing for all cohorts.



Planned Phase 1 Clinical Trial (United States)

We also plan to initiate a randomized, masked Phase 1 clinical trial of up to 20 subjects in the United States under an eIND application in mid-2021 to evaluate 15 subjects dosed with a 600 µg dose of OTX-TKI in comparison to 5 subjects receiving a 2 mg dose of aflibercept every eight weeks for the treatment of wet AMD, DME and RVO. The clinical trial will evaluate biological activity, as measured by CSFT and BCVA, tolerability and durability. We have requested a pre-IND meeting with the FDA to discuss a possible plan to transition from an eIND application to a traditional IND application.

Planned Phase 2 Clinical Trial (Australia)

Pending our receipt and review of the topline data from the Phase 1 clinical trial in Australia and related regulatory discussions, we plan to initiate a Phase 2 clinical trial in Australia to compare the administration of a single dose of 600 µg OTX-TKI in combination with an anti-VEGF induction injection of a 2 mg dose of aflibercept, a current standard of care anti-VEGF therapy, to a 2mg dose of aflibercept alone as the comparator. The Phase 2 clinical trial is anticipated to include approximately 100 subjects with wet AMD but who have responded to current standard of care anti-VEGF treatment and currently show an absence of fluid. The Phase 2 clinical trial will be designed to evaluate efficacy, as measured by CSFT and BCVA, tolerability and durability.

Regulatory Pathway

If we receive positive data from the Phase 1 clinical trial in the United States, we plan to initiate a Phase 2 clinical trial and two Phase 3 clinical trials in the United States for the treatment of wet AMD, DME and RVO. 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.

OTX-AFS (aflibercept suprachoroidal implant) in Collaboration with Regeneron

Regeneron Collaboration Agreement

In October 2016, we entered into a strategic collaboration, option and license agreement with Regeneron for the development and potential commercialization of products using our extended-delivery hydrogel formulation in combination with Regeneron's large molecule VEGF-targeting compounds for the treatment of retinal diseases, with the initial focus on the VEGF trap aflibercept, currently marketed under the brand name Eylea. We and Regeneron amended this agreement in May 2020 to, among other things, transition joint efforts under the collaboration to the research and development of an extended-delivery formulation of aflibercept to be delivered to the suprachoroidal space. We refer to the collaboration, option and license agreement, as amended to date, as the Collaboration Agreement.

Under the terms of the Collaboration Agreement, we granted Regeneron an option, or the Option, to enter into an exclusive, worldwide license under our intellectual property to develop and commercialize products using our hydrogel in combination with Regeneron's large molecule VEGF-targeting compounds, or Regeneron Licensed Products. The Collaboration Agreement does not cover the development of any products that deliver small molecule drugs, including TKIs, for any target including VEGF, or any products that deliver large molecule drugs other than those that target VEGF proteins. Under the terms of the Collaboration Agreement, we and Regeneron agreed to conduct a joint research program with the aim of developing an extended-delivery formulation of aflibercept that is suitable for advancement into clinical development. Regeneron has agreed to pay our personnel and material costs of ours for specified preclinical development activities in connection with the revised workplan, as well as costs of certain specialty equipment.

Under the terms of the Collaboration Agreement, Regeneron is responsible for funding an initial preclinical tolerability study. If the Option is exercised, Regeneron will be obligated to conduct further preclinical development and an initial clinical trial under a collaboration plan. We are obligated to reimburse Regeneron for certain development costs during the period through the completion of the initial clinical trial, subject to a cap of $25 million, which cap may be increased by up to $5 million under certain circumstances. We do not expect our funding requirements under the collaboration to be material over the next twelve months. If Regeneron elects to proceed with further development beyond the initial clinical trial, it will be solely responsible for conducting and funding further development and commercialization of product candidates. If the Option is exercised, Regeneron is required to use commercially reasonable efforts to research, develop and commercialize at least one Regeneron Licensed Product. Such efforts shall include initiating the dosing phase of a subsequent clinical trial within specified time periods following the completion of the first-in-human clinical trial or the initiation of preclinical toxicology studies, subject to certain extensions.

Under the terms of the Collaboration Agreement, Regeneron has agreed to pay us $10 million upon exercise of the Option. If Regeneron elects to exercise the Option, we are also eligible to receive up to $145 million per Regeneron Licensed Product upon the achievement of specified development and regulatory milestones, including successful results from the first-in-human clinical trial; $100 million per Regeneron Licensed Product upon first commercial sale of such Regeneron Licensed Product; and up to $50 million based on the achievement of specified sales milestones for all Regeneron Licensed Products. In addition, we are entitled to 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.

As amended, the Option is exclusive for twenty-four months following May 8, 2020. The field of the potential license remains limited to Regeneron Licensed Products delivered by local administration to or around the eye for diagnostic, therapeutic, or prophylactic purposes relating to ophthalmic diseases or conditions.

The Collaboration Agreement will automatically terminate upon the failure of Regeneron to conduct or complete certain preclinical activities within specified timeframes or provide required notices regarding such certain preclinical activities to us, in each case subject to specified exceptions, unless Regeneron exercises its Option, the matter has been referred to the joint research committee, or the parties have otherwise agreed in writing. The Agreement will also terminate if Regeneron has not exercised its Option prior to the expiration of the Option Period. If Regeneron has timely exercised its Option, the Collaboration Agreement will expire on a Regeneron Licensed Product-by-Regeneron Licensed Product and country-by-country basis upon the expiration of the later of 10 years from the date of first commercial sale in such country or the expiration of all patent rights covering a Regeneron Licensed Product in such country. We have agreed to grant Regeneron a fully paid-up, non-exclusive license to continue to develop and commercialize the Regeneron Licensed Products following expiration. The Collaboration Agreement is terminable by Regeneron at its convenience, for any or all of the Regeneron Licensed Products, upon prior written notice. Either party may, subject to a

cure period, terminate the Collaboration Agreement in the event of the other party's uncured material breach, in addition to other specified termination rights.

Glaucoma Program

OTX-TIC (travoprost intracameral implant)

Our development efforts for our glaucoma program have focused on the use of our extended-delivery hydrogel in combination with travoprost, an FDA-approved prostaglandin analog designed to lower elevated IOP. Our product candidate OTX-TIC is a bioresorbable hydrogel implant incorporating travoprost that is designed to be administered by a physician as an intracameral injection into the anterior chamber of the eye with an initial target duration of drug release of four to six months.

In Vitro and Preclinical results

Preclinical studies to date have demonstrated clinically meaningful IOP lowering and good pharmacokinetics in the aqueous humor.

Phase 1 clinical development

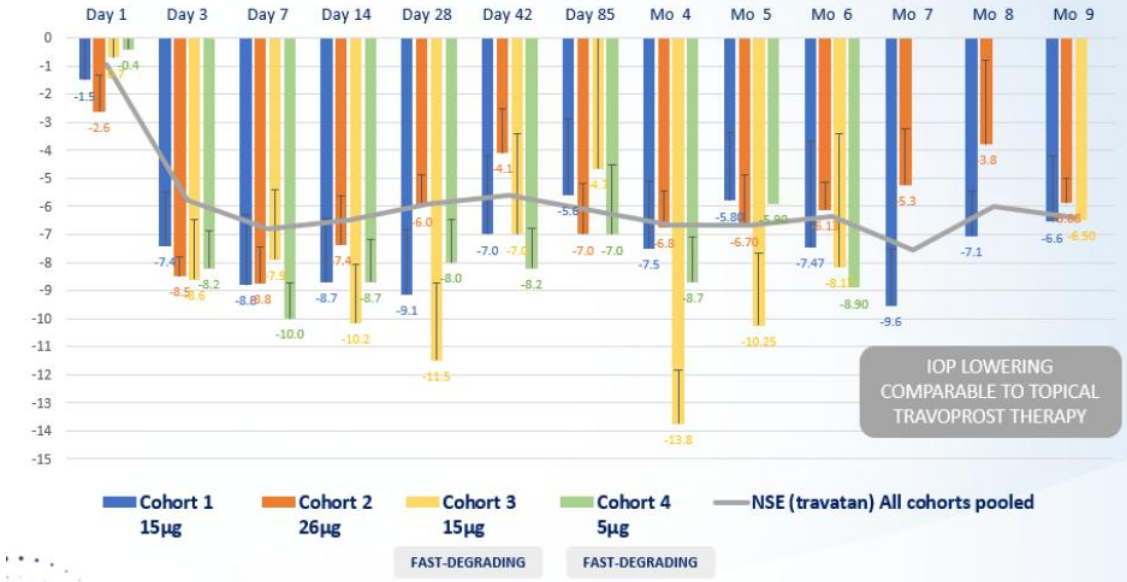
We are conducting a prospective, multi-center open-label, dose-escalation proof-of-concept Phase 1 clinical trial of OTX-TIC in the United States that we initiated in the second quarter of 2018 for the treatment of patients with moderate to severe glaucoma or ocular hypertension. The clinical trial is designed to evaluate the safety, biological activity, durability and tolerability of OTX-TIC compared to topical travoprost (daily eye drops) in patients with open-angle glaucoma or ocular hypertension. The clinical trial consists of four patient cohorts: cohort 1 is 5 subjects who are receiving a 15 µg dose, cohort 2 is 4 subjects who are receiving a 26 µg dose, cohort 3 is 5 subjects who are receiving a 15 µg dose with a fast-degrading implant, and cohort 4 is 5 subjects who are receiving a 5 µg dose with a fast-degrading implant. We presented initial results from the first cohort, comprised of five patients, in this clinical trial at the Association of Research and Vision of Ophthalmology (ARVO) meeting in April 2019 and the American Society of Cataract and Refractive Surgery annual meeting in May 2019. This data demonstrated that, with a single implant, subjects were able to achieve IOP lowering for up to thirteen months at a level at least as good as standard of care topical eye drop that was placed in each subject's non-study eye. In addition, the hydrogel carrier, as designed, biodegraded in five to seven months. There were no clinically meaningful changes in corneal health as measured by endothelial cell evaluation and corneal pachymetry. Several subjects reported low-grade inflammation and peripheral anterior synechiae that we believe may be addressable with modifications to the implants.

At the Glaucoma360 2021 Virtual Conference, we presented interim results, presented below, from all four patient cohorts in the Phase 1 clinical trial. We believe that OTX-TIC shows potential as a sustained-release therapy with a long duration of action. OTX-TIC has demonstrated a clinically meaningful mean change from baseline as measured by IOP at 8:00 am, 10:00 am and 4:00 pm comparable to topical travoprost therapy as early as two days following injection across all four cohorts. With regard to duration, three out of five subjects (60%) in cohort 1 and four out of four subjects (100%) in cohort 2 exhibited duration of IOP-lowering effect comparable to travoprost therapy at six months. Two out of five subjects (40%) in cohort 3 and one out of 2 subjects (50%) in cohort 4 assessed to date exhibited duration of IOP-lowering effect comparable to travoprost at six months.

The OTX-TIC implant was observed to biodegrade in between five and seven months in cohorts 1 and 2. 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 patients using gonioscopy. Corneal health as measured by endothelial cell counts, pachymetry assessments, and slit lamp examinations indicated no clinically meaningful changes from baseline in any of the four cohorts. IOP elevation were observed in three subjects in cohort 3 at the approximate time of the implant resorption.

ALL COHORTS: MEAN IOP CHANGE FROM BASELINE

IOP DECREASED AFTER 2 DAYS FOLLOWING OTX-TIC IMPLANTATION & LOWERING TO 7-11 MMHG RECORDED



NB: Interim look as of 01/12/2021. Unmonitored data (8AM measurements). If the study eye was given other IOP lowering medication, the IOP value was removed from the analysis.

ALL COHORTS: DURATION OF EFFECT WITH ONE IMPLANT

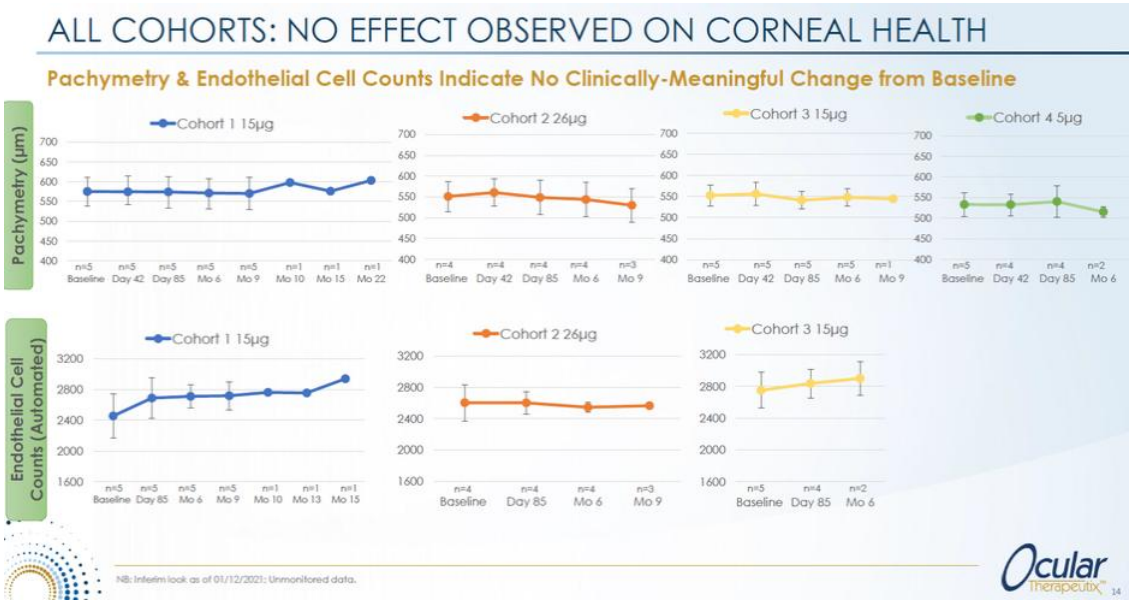
Cohort 2 Showed the Most Consistent Durable Response in all Subjects up to Month 6 & 50% of Subjects up to Month 9

	Day 42 % (n/N)	Day 85 % (n/N)	Month 4 % (n/N)	Month 5 % (n/N)	Month 6 % (n/N)	Month 7 % (n/N)	Month 8 % (n/N)	Month 9 % (n/N)	Month 10-22 % (n/N)
Cohort 1 (15 µg) N=5	100(5/5)	100(5/5)	80(4/5)	80(4/5)	60(3/5)	40 (2/5)	40 (2/5)	40 (2/4)	20 (1/5)
Cohort 2 (26 µg) N=4	100(4/4)	100(4/4)	100(4/4)	100(4/4)	100(4/4)	100(4/4)	75(3/4)	50(2/4)	NA
Cohort 3 (15 µg) (Fast-degrading) N=5	100(5/5)	60(3/5)	40 (2/5)	40 (2/5)	40 (2/5)	20 (1/5)	20 (1/5)	20 (1/5)	NA
Cohort 4 (5 µg) (Fast-degrading) N=5[1]	100(4/4)	100(4/4)	75(3/4)	75(3/4)	50(1/2)	NA	NA	NA	NA
Total[1]	100 (18/18)	89 (16/18)	72 (13/18)	72 (13/18)	63 (10/16)	50 (7/14)	43 (6/14)	39 (5/13)	20 (1/5)

<50% 50-74% 75-99% 100%

NB: Interim look as of 01/12/2021. Unmonitored data (8AM measurements)
[1]Ongoing follow-up

Ocular Therapeutix™



Planned Phase 2 Clinical Trial

In mid-2021, we plan to initiate a Phase 2 clinical trial to evaluate formulations of OTX-TIC for the treatment of open-angle glaucoma or ocular hypertension in patients. Certain subjects in the Phase 2 clinical trial will receive the same formulation used in cohort 1 of the Phase 1 clinical trial, containing a 26 µg dose of drug and utilizing a standard implant, and others will receive 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. The Phase 2 clinical trial will be a randomized, double-masked, active-controlled study with a total of approximately 105 subjects between three arms of approximately 35 subjects each. The control arm will receive an injection of Durysta™. The non-study eye of each patient will receive topical prostaglandin daily. The trial will evaluate IOP changes from baseline among other endpoints.

Regulatory Pathway

If our planned Phase 2 clinical trial is successful, we would then be required to successfully complete two well-controlled Phase 3 clinical trials conducted under an IND to obtain marketing approval from the FDA. If we were to obtain favorable results from these two pivotal clinical trials, we expect that we would submit an NDA to the FDA for marketing approval of OTX-TIC under Section 505(b)(2) of the FDCA. See "—Government Regulation—Section 505(b)(2) NDAs."

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 initial development efforts are focused on the use of our extended-delivery hydrogel in combination with well-known and well-understood corticosteroids and cyclosporine for the treatment of dry eye disease, allergic conjunctivitis and inflammation and pain following ophthalmic surgery.

Dry Eye Disease

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 patients 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 to increase tear production for the chronic treatment of dry eye disease.

Phase 1 clinical development

We filed 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 corneal total fluorescein staining (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 patients in a 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 is a U.S.-based, randomized, double-masked, multi-center, vehicle-controlled trial evaluating two different formulations of OTX-CSI compared with a hydrogel vehicle insert in approximately 140 subjects who are to be followed for a period of 16 weeks. Included patients must have been diagnosed with dry eye disease in both eyes for a period of greater than six months and have a visual analog scale, or 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 corneal fluorescein staining and symptoms of dry eye disease as measured by the VAS eye dryness severity score and the VAS dry eye frequency score.

Regulatory Pathway

We anticipate receiving topline data from our ongoing Phase 2 clinical trial in the fourth quarter of 2021. If our planned Phase 2 clinical trial is successful, we would then be required to successfully complete two well-controlled Phase 3 clinical trials conducted under an IND to obtain 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.

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 a 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 use of corticosteroids for dry eye disease have limited widespread adoption. We believe that 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, its preservative-free active pharmaceutical ingredient, into a hydrogel, drug-eluting intracanalicular insert. OTX-DED incorporates the same active drug as DEXTENZA, but it includes a lower dose of the drug, delivers it via a smaller insert, and is designed to release it over a period of two to three weeks.

Phase 2 clinical trial

We filed an IND in December 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 hydrogel implant in a total of approximately 150 subjects with dry eye disease, approximately 50 patients per arm. The subjects will be followed for approximately two months after randomization. This trial is 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 patients will be required to have diagnosed dry eye disease in both eyes for at least six months, a VAS eye dryness severity score of at least 30 and bulbar conjunctival hyperemia grade of at least 2 (Cornea Contact Lens Research Unit scale). The primary endpoint is mean change in bulbar conjunctival hyperemia from baseline measured at 15 days post treatment by central reading center photographic assessment. Secondary endpoints include eye dryness symptoms using VAS, total corneal fluorescein staining using the National Eye Institute scale and adverse events, both ocular and non-ocular.

Regulatory Pathway

We anticipate receiving topline data from our ongoing Phase 2 clinical trial in the first half of 2022. If our planned Phase 2 clinical trial is successful, we would then be required to successfully complete two well-controlled Phase 3 clinical trials conducted under an IND to obtain 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.

Allergic Conjunctivitis

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 and designed to release the FDA-approved corticosteroid dexamethasone to the ocular surface for up to 30 days.

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 anti-histamine 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 could 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.

Completed Phase 2 Clinical Trial

In November 2014, we completed a prospective, randomized, parallel-arm, vehicle-controlled, multicenter, double-masked Phase 2 clinical trial evaluating the safety and efficacy of DEXTENZA for the treatment of allergic conjunctivitis. We conducted this trial using a modified version of a controlled exposure model commonly used to assess anti-allergy medications, Ora, Inc.'s modified Conjunctival Allergen Challenge (Ora-Cac®), which we refer to as the CAC Model. The modified CAC achieves a very high transient dose exposure by placing allergen directly into the space between the eyelid and the surface of the eye of the patient. We initially exposed patients to specified allergens to determine which allergens resulted in an allergic response for the patients. If patient was responsive to a particular allergen, we continued to expose the patient to that same allergen prior to each evaluation.

We enrolled 68 patients at two sites in the United States. We randomized patients in a 1:1 ratio to receive either DEXTENZA or a placebo vehicle control intracanalicular insert without active drug. We evaluated patients using three

allergen challenges in series for each of the two efficacy measures at 14, 28 and 42 days following placement of the intracanalicular insert.

The primary efficacy measures for this trial were ocular itching graded by the patient and conjunctival redness graded by the trial investigator, in each case based on a five point scale from zero to four. The primary efficacy measures were differences between treatment groups of at least 0.5 units on the five point scale on day 14 for all three time points measured in a day for both ocular itching and conjunctival redness and differences between treatment groups of at least 1.0 unit for the majority of the three time points measured on 14 days post insertion for both ocular itching and conjunctival redness. The secondary endpoints for this trial were similar to the primary efficacy endpoints, except that each variable was assessed at 28 days and 42 days following placement of the intracanalicular insert.

We enrolled patients in this trial who were at least 18 years of age with a positive history of ocular allergies and a positive skin test reaction to a perennial allergen and a seasonal allergen. We excluded patients from this trial if, among other reasons, they had an active ocular infection or itching or conjunctival redness at screening.

We evaluated safety in all patients at each study visit with an assessment of general eye conditions, including visual acuity and IOP, along with any adverse events.

Efficacy: In this trial, there was a statistically significant mean difference ($p<0.05$) between the DEXTENZA treatment group and the vehicle group for both ocular itching and conjunctival redness at all three time points measured on 14, 28, and 42 days following placement of the intracanalicular insert. DEXTENZA met one of the two primary efficacy endpoints. The DEXTENZA treatment group achieved a mean difference compared to the vehicle control group of more than 0.5 units on a five point scale at 14 days post insertion for all three time points measured in a day for both ocular itching and conjunctival redness. The DEXTENZA group did not achieve a mean difference compared to the vehicle control group of 1.0 unit for the majority of the three time points measured on 14 days post insertion for either ocular itching or conjunctival redness. However, in a pre-specified analysis group of a second site in the clinical trial, in which DEXTENZA intracanalicular inserts were placed 48 to 72 hours following exposure to the allergen, rather than on the same day, we observed a mean difference in ocular itching between the DEXTENZA group and the vehicle control group of approximately 1.0 unit for the majority of three time points measured on 14 days.

The results of this trial for each of the three time points on day 14 following the insertion of the intracanalicular insert for the DEXTENZA group and the vehicle control group are shown in the table below:

Parameter	Time Point	DEXTENZA	Vehicle	Treatment Difference (P-value)
Ocular Itching	3 min	1.80 (1.068)	2.58 (0.823)	**-0.78 (0.0031)**
	5 min	1.72 (0.998)	2.70 (0.865)	**-0.98 (0.0002)**
	7 min	1.65 (0.989)	2.53 (0.880)	**-0.88 (0.0007)**
Conjunctival Redness	7 min	1.60 (0.753)	2.11 (0.727)	**-0.51 (0.0100)**
	15 min	1.53 (0.753)	2.23 (0.708)	**-0.70 (0.0006)**
	20 min	1.54 (0.739)	2.21 (0.696)	**-0.67 (0.0008)**

Safety: In this trial, there was one serious adverse event in the treatment arm, which was depression. This event was not suspected to be related to treatment. The serious adverse event was not ocular in nature. In addition, there were a variety of adverse events in both the DEXTENZA group and the vehicle control group, with nine ocular adverse events and two non-ocular related adverse events in the DEXTENZA group and eight ocular adverse events and two non-ocular adverse events in the vehicle control group. In the DEXTENZA group, the only adverse events that occurred more than once were reduction in visual acuity and increased IOP, both of which occurred twice. The most common adverse events in the vehicle control group were erythema of the eyelid, discharge from the eye and an increase in lacrimation, all of which occurred twice. All adverse events were transient in nature and completely resolved by the end of the trial.

Phase 3 Clinical Program

We met with the FDA in December 2014 to review the Phase 2 clinical trial results of DEXTENZA for the treatment of allergic conjunctivitis and to discuss our planned Phase 3 clinical development program. Based on these discussions, we have completed two Phase 3 clinical trials and initiated a third Phase 3 clinical trial in August 2019. Our first Phase 3 clinical trial assessed both ocular itching and conjunctival redness associated with allergic conjunctivitis. Our second and third Phase 3 clinical trials have focused on the ocular itching indication.

First Phase 3 Clinical Trial

We initiated our first planned Phase 3 clinical trials in June 2015, and we reported topline efficacy results in October 2015. This first Phase 3 clinical trial was a prospective, randomized, parallel-arm, vehicle-controlled, multicenter, double-masked trial. A total of 73 patients were enrolled in this trial and were randomized in a 1:1 ratio to receive either DEXTENZA or a placebo vehicle control intracanalicular insert without active drug. This trial was conducted using the CAC Model. We evaluated patients using three allergen challenges in series for each of two efficacy measures at days 7, 14 and 28 following placement of intracanalicular insert as described below. In this Phase 3 clinical trial, we placed the intracanalicular inserts 48 to 72 hours after exposure to the allergen. In our completed Phase 2 clinical trial, we obtained better efficacy results with this design protocol as noted in the description of the Phase 2 efficacy results above.

The primary efficacy measures for this trial were ocular itching graded by the patient and conjunctival redness graded by the trial investigator, in each case based on a five point scale from zero to four. The primary efficacy endpoints were the differences between the treatment group and the vehicle group of at least 0.5 units on the five point scale measured on 7 days post-insertion of the intracanalicular insert for all three time points measured for both ocular itching and conjunctival redness and differences of at least 1.0 unit for the majority of the three time points measured on 7 days post-insertion of the intracanalicular insert for both ocular itching and conjunctival redness. The secondary endpoints were similar to the primary efficacy endpoints except that each variable was assessed at day 14 and day 28 following insertion of the intracanalicular insert. The primary efficacy measure of conjunctival redness is typically included in Phase 3 trials for allergic conjunctivitis but has not been required for FDA approval of drugs for allergic conjunctivitis. Most commercially available prescription medications for the treatment of allergic conjunctivitis have an ocular itching indication only. As described below, ocular itching was the only primary efficacy endpoint in the second Phase 3 trial of DEXTENZA for the treatment of allergic conjunctivitis, with conjunctival redness being moved to a secondary efficacy endpoint.

We enrolled patients in this trial who were at least 18 years of age with a positive history of ocular allergies and a positive skin test reaction to a perennial allergen and a seasonal allergen. We excluded patients from this trial if, among other reasons, they had an active ocular infection or itching or conjunctival redness at screening.

We evaluated safety in all patients at each study visit with an assessment of general eye conditions, including visual acuity and IOP, along with any adverse events.

Efficacy: In this trial, there was a statistically significant mean difference ($p<0.0001$) between the DEXTENZA treatment group and the placebo vehicle group for ocular itching at all three time points measured on 7 days post-placement of the intracanalicular insert. DEXTENZA also met the primary efficacy endpoint for ocular itching. The DEXTENZA treatment group achieved a mean difference compared to the vehicle group of greater than 0.5 units on a five point scale on 7 days post-insertion at each time point and greater than 1.0 unit at a majority of the time points on 7 days post-insertion for ocular itching. There was a statistically significant mean difference ($p=0.01$ or less) between the DEXTENZA treatment group and the placebo vehicle group for conjunctival redness at all three time points measured on 7 days post-placement of the intracanalicular insert. However, the DEXTENZA group did not achieve the pre-specified primary efficacy endpoints on 7 days post-insertion with respect to conjunctival redness.

The results of this trial for each of the three time points on day 7 following placement of the intracanalicular insert for the DEXTENZA group and the vehicle control group are shown in the table below:

Parameter	Time Point	DEXTENZA	Vehicle	Treatment Difference (P-value)
Ocular Itching	3 min	1.68 (1.032)	2.66 (0.861)	**-1.02 (<0.0001)**
	5 min	1.87 (1.04)	2.74 (0.69)	**-0.87 (<0.0001)**
	7 min	1.70 (0.938)	2.74 (0.679)	**-1.04 (0.0007)**
Conjunctival Redness	7 min	1.52 (0.641)	1.80 (0.764)	**-0.26 (0.1082)**
	15 min	1.48 (0.698)	1.75 (0.786)	**-0.32 (0.0419)**
	20 min	1.44 (0.710)	1.76 (0.766)	**-0.29 (0.0667)**

Safety: There were no serious adverse events reported in this trial. There were a variety of adverse events in both the DEXTENZA group and the vehicle control group, with three patients in the DEXTENZA treatment group with a total of three ocular adverse events and one non-ocular adverse event and four patients in the vehicle control group with a total of six ocular adverse events and one non-ocular adverse events. The most common ocular adverse event was increased lacrimation, which was experienced by one patient in the DEXTENZA group and two patients in the vehicle control group. Other treatment-related ocular adverse events included increased IOP in the DEXTENZA group, and blepharospasm in the vehicle control group.

Second Phase 3 Clinical Trial

We initiated our second Phase 3 clinical trial of DEXTENZA for the treatment of allergic conjunctivitis in November 2015, and we reported topline efficacy results in June 2016. This second Phase 3 clinical trial was a prospective, randomized, parallel-arm, vehicle-controlled, multicenter, double-masked trial. A total of 72 patients were enrolled in this trial and randomized in a 1:1 ratio to receive either DEXTENZA or a placebo vehicle control intracanalicular insert without active drug. This trial was conducted using the CAC Model. Patients were evaluated using three allergen challenges in series for each of two efficacy measures at days 7, 14 and 28 following insertion of the intracanalicular insert. In this Phase 3 clinical trial, we placed the intracanalicular inserts 48 to 72 hours after exposure to the allergen.

The single primary efficacy measure for this trial was ocular itching graded by the patient based on a five point scale from zero to four. The primary efficacy endpoints were the differences between the treatment group and the vehicle group of at least 0.5 units on the five point scale 7 days post-insertion of the intracanalicular insert for all three time points measured for ocular itching and differences of at least 1.0 unit for the majority of the three time points measured 7 days post-insertion of the intracanalicular insert for ocular itching. The secondary endpoints for ocular itching were similar to the primary efficacy endpoints except that each variable was assessed at day 14 and day 28 following placement of the intracanalicular insert. The secondary endpoints for conjunctival redness were the differences between the treatment group and the vehicle group of at least 0.5 units on the five point scale 7 days post-insertion of the intracanalicular insert for all three time points measured and differences of at least 1.0 unit for the majority of the three time points measured 7 days post-insertion of the intracanalicular insert.

We enrolled patients in this trial who are at least 18 years of age with a positive history of ocular allergies and a positive skin test reaction to a perennial allergen and a seasonal allergen. We excluded patients from this trial if, among other reasons, they had an active ocular infection or itching or conjunctival redness at screening.

We evaluated safety in all patients at each study visit with an assessment of general eye conditions, including visual acuity and IOP, along with any adverse events.

Efficacy: In this trial, DEXTENZA did not meet the primary efficacy endpoint of ocular itching at the three time points measured on day 7 post-placement of the intracanalicular insert. The mean difference in ocular itching in the

DEXTENZA treatment group compared to the placebo group measured 7 days following insertion of the inserts, at 3, 5, and 7 minutes was -0.18, -0.29, and -0.29 units, respectively, on a five point scale and did not achieve statistical significance. In addition, the trial did not achieve the requirement of at least a 0.5 unit difference at all three time points 7 days following insertion of the inserts and at least a 1.0 unit difference at a majority of the three time points between the treatment group and the placebo group 7 days following insertion of the inserts.

The trial also assessed conjunctival redness as a secondary endpoint. The differences in the mean scores in conjunctival redness between the DEXTENZA treatment group and the placebo group 7 days following insertion of the inserts at 7, 15 and 20 minutes were -0.35, -0.39 and -0.42, respectively.

The results of this trial for each of the three time points on day 7 following placement of the intracanalicular insert for the DEXTENZA group and the vehicle control group are shown in the table below:

Parameter	Time Point	DEXTENZA	Vehicle	Treatment Difference* (P-value)
Ocular Itching	3 min	2.04 (1.088)	2.31 (1.115)	**-0.18 (0.44)**
	5 min	2.07 (1.1)	2.41 (1.039)	**-0.29 (0.223)**
	7 min	2.02 (1.131)	2.37 (1.129)	**-0.29 (0.2611)**

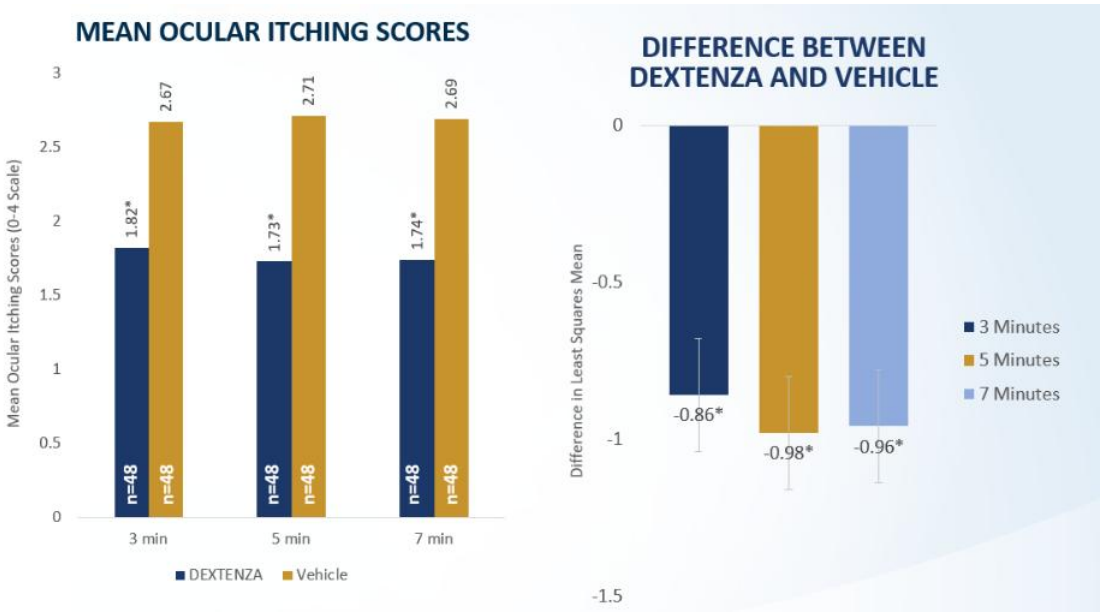
Safety: There were no serious adverse events reported in this trial. There were a variety of adverse events in both the DEXTENZA group and the vehicle control group, with six patients in the DEXTENZA treatment group with a total of six ocular and one non-ocular adverse events and 11 patients in the vehicle control group with a total of nine ocular and eight non-ocular adverse events. The lower rate of ocular adverse events in the DEXTENZA group could potentially be due to the presence of an anti-inflammatory active pharmaceutical ingredient. Ocular adverse events reported more than one patient in either treatment group included increased IOP, which was experienced by two patients in the DEXTENZA group, as well as dacryostenosis acquired and dacryocanaliculitis, each experienced by two patients in the vehicle control group. Both cases of IOP increased were considered treatment related, as were both cases of dacryocanaliculitis and a single case of dacryostenosis. All other ocular adverse events were reported by single patients in either the DEXTENZA or vehicle control group, with most in the PV group considered treatment related.

Third Phase 3 Clinical Trial

In the third quarter of 2019, we began dosing patients in a 96-subject, pivotal Phase 3 clinical trial evaluating DEXTENZA for the treatment of ocular itching associated with allergic conjunctivitis. This Phase 3 clinical trial was a U.S.-based, multi-center, 1:1 randomized, double-masked, placebo-controlled trial designed to evaluate the safety and efficacy of DEXTENZA versus a punctum plug using the CAC Model. The trial was designed to assess the effect of DEXTENZA compared with a placebo on allergic reactions using a series of successive allergen challenges over a 30-day period. The primary efficacy endpoint for this trial was ocular itching (subject-reported 5-point scale (0 to 4)) on day 8 at 3 minutes, 5 minutes and 7 minutes post-challenge and included subjects with seasonal and perennial allergens.

Efficacy: DEXTENZA-treated subjects demonstrated a statistically significant (p-value < 0.0001) difference in mean ocular itching scores, compared to vehicle-treated subjects, at all three pre-specified time points (see the figure below). An assessment of the secondary endpoint of ocular itching at all other visits (day 7, day 8 (morning), day 8 (afternoon at 10 minutes following exposure), day 14, and day 15 (morning and afternoon)) also showed that DEXTENZA-treated subjects reported lower itching scores than vehicle-treated subjects at 3 minutes, 5 minutes, 7 minutes and 10 minutes post-exposure to the allergen challenge (p-value <0.05 for all 21 time points except day 7 at 3 minutes).

Primary Efficacy Endpoint Ocular Mean Itching Scores at Day 8 (PM)



*Statistically significant; P≤0.0001; Least Squared Means; Population: ITT = MCMC; Bars represent Standard Error

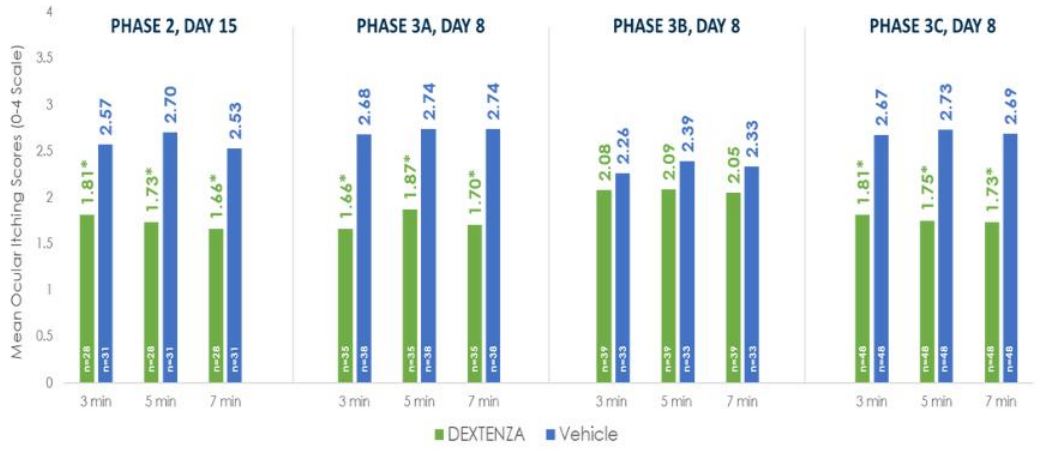
Safety: In the trial, DEXTENZA was generally observed to have a favorable safety profile and be well-tolerated. No serious adverse events were observed. No subjects required rescue medication and no subjects experienced elevated IOP. There were 8 ocular treatment-emergent adverse events in this trial (2 in the DEXTENZA group and 6 in the vehicle group).

Overview of clinical trial data

Data received from the third Phase 3 clinical trial evaluating DEXTENZA for ocular itching associated with allergic conjunctivitis was generally consistent with our observations in our prior Phase 2 and Phase 3a clinical trials using a similar repeat CAC Model as reflected in the two figures below. For all analyses we have conducted, the subject is the unit of analysis. For the Phase 2 clinical trial, the data shown is for the prespecified primary endpoint of ocular itching at day 15 using the Intent-to-Treat (ITT) population and utilizing the last observation carried forward (LOCF) methodology to impute missing data. For the Phase 3 trials, the data shown is for the prespecified primary endpoint of ocular itching at day 8 using the ITT population and imputing missing data using the Markov Chain Monte Carlo (MCMC) multiple imputation method. The two figures below reflect the Phase 3 data using the MCMC method with different bases for imputation. In the first figure, the basis for imputation for the MCMC method is at the individual eye level. In the second figure, the basis for imputation for the MCMC method is at the subject level (average of the two eyes). Both methods may be appropriate and, in this case, yield similar conclusions. In certain data we have previously disclosed, we have presented analyses using the MCMC method with the individual eye as the basis for imputation. However, the statistical analysis plan for each of the three Phase 3 trials specifies that the basis for imputation for the MCMC method should be the subject level. Multiple other methods of imputation were also performed in some of the Phase 3 studies—including LOCF, baseline observation carried forward (BOCF), worse case observation (WCO), and observation only with no imputation—with similar clinical conclusions.

Primary Efficacy Endpoint – Eye Level Imputation

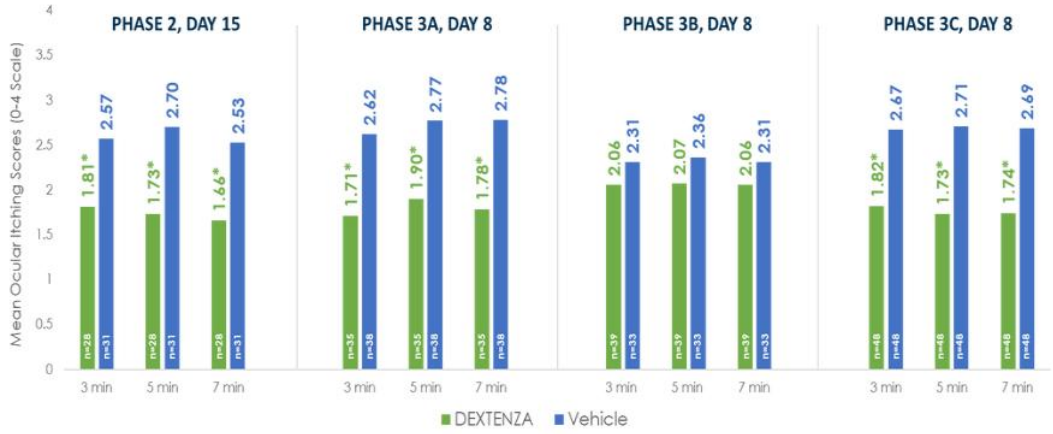
Mean Ocular Itching Scores Across All Studies



* Statistically Significant; P≤0.0025; Population: ITT + LOCF (Phase 2) & ITT + MCMC (Phase 3)

Primary Efficacy Endpoint – Subject Level Imputation

Mean Ocular Itching Scores Across All Studies



* Statistically Significant; P≤0.0025; Population: ITT + LOCF (Phase 2) & ITT + MCMC (Phase 3)

Regulatory Pathway

In the fourth quarter of 2020, we submitted an sNDA for DEXTENZA under Section 505(b)(2) of the FDCA (See "—Government Regulation—Section 505(b)(2) NDAs" for additional information) to include the treatment of ocular itching associated with allergic conjunctivitis as an additional approved indication. The FDA has accepted our sNDA for filing and has established a target action date under PDUFA of October 18, 2021. We believe that the totality of the efficacy and safety data across the Phase 2 trial and the three Phase 3 trials (n = 323 subjects), as well as the safety data associated with the prior approval of DEXTENZA for the treatment of inflammation and pain following ophthalmic surgery, represent a strong data package in support of the sNDA.

If our sNDA is approved, we expect to launch DEXTENZA for the treatment of ocular itching associated with allergic conjunctivitis in the first half of 2022.

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.

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.

Embedded within our DEXTENZA intracanalicular insert are dexamethasone drug particles that 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.

Overview of Clinical Development for Post-Surgical Ocular Inflammation and Pain

In March and April 2015, we reported topline results from two Phase 3 clinical trials for the treatment of post-surgical ocular inflammation and pain. In the first Phase 3 clinical trial, DEXTENZA met both primary efficacy endpoints, absence of pain at day 8 and absence of inflammatory cells at day 14, with statistical significance. In the second Phase 3 clinical trial, DEXTENZA met the primary efficacy endpoint for absence of pain at day 8 with statistical significance but did not meet the primary efficacy endpoint for absence of inflammatory cells at day 14. We met with the FDA in April 2015 to discuss the path forward for seeking marketing approval of DEXTENZA for the treatment of post-surgical ocular inflammation and pain.

In this pre-NDA clinical meeting, the FDA indicated that the existing data from our Phase 2 and two Phase 3 clinical trials are appropriate to support an NDA submission for DEXTENZA for a post-surgical ocular pain indication. The FDA further indicated that we would need additional data from a third Phase 3 clinical trial for the inflammation endpoint to support the potential labeling expansion of DEXTENZA's indications for use. We initiated a third Phase 3 clinical trial for DEXTENZA for the treatment of post-surgical ocular inflammation and pain in October 2015. In September 2015, we submitted to the FDA an NDA for DEXTENZA for the treatment of post-surgical ocular pain. In July 2016, we received a complete response letter, or CRL, from the FDA regarding our NDA for DEXTENZA. We

resubmitted our NDA for DEXTENZA for the treatment of post-surgical ocular pain in June 2018. In November 2018, we received approval for the pain indication. In June 2019, we received approval for the inflammation indication.

Completed Phase 3 Clinical Trials

In 2014, we initiated a pivotal clinical trial program that consisted of two prospective, randomized, parallel-arm, vehicle-controlled, multicenter, double-masked Phase 3 clinical trials evaluating the safety and efficacy of DEXTENZA for the treatment of ocular inflammation and pain following cataract surgery. We initiated the first of these Phase 3 clinical trials in February 2014 and the second trial in April 2014. Patient enrollment was completed in September 2014, and the topline efficacy data from these clinical trials was reported in March and April 2015. We initiated a third Phase 3 clinical trial in the October 2015. Patient enrollment in the third Phase 3 clinical trial was completed in May 2016 and the topline efficacy data was reported in November 2016.

We enrolled 247 patients at 16 sites in the first Phase 3 clinical trial, 241 patients at 16 sites in the second Phase 3 clinical trial and 438 patients at 21 sites in the third Phase 3 clinical trial in the United States pursuant to our effective IND. We randomized patients in a 2:1 ratio in the first two Phase 3 clinical trials and in a 1:1 ratio in the third Phase 3 clinical trial to receive either DEXTENZA or a placebo vehicle control intracanalicular insert without active drug. We evaluated patients at days 2, 4, 8, 14, 30 and 60 following surgery in the first two Phase 3 trials and at days 2, 4, 8, 14, and 30 in the third Phase 3 clinical trial.

The two primary efficacy measures in these trials were absence of inflammatory cells in the anterior chamber of the study eye when measured with a slit lamp biomicroscope and absence of pain in the study eye. To meet the efficacy end point for absence of inflammatory cells, there needed to be a complete absence of inflammatory cells. In these trials, absence of pain was based on a patient reported score of zero on a scale from zero to ten of ocular pain assessment. The first primary efficacy endpoint for these trials was the difference in the proportion of patients in each treatment group with absence of inflammatory cells in the anterior chamber of the study eye at day 14 following surgery. Pivotal clinical trials for other ophthalmic steroid drugs approved by the FDA for marketing in the United States also have evaluated this endpoint at day 14. The second primary efficacy endpoint for these trials was the difference in the proportion of patients in each treatment group with absence of pain in the study eye at day 8 following surgery. For clarification of the endpoints, the day of surgery and insertion of DEXTENZA or the placebo is considered to be day 1.

We evaluated as secondary efficacy measures the level of flare, an indicator of inflammation in the anterior chamber of the study eye at each evaluation date until day 30 and absence of inflammatory cells in the anterior chamber of the study eye and absence of pain in the study eye at each evaluation date other than the day used for the primary efficacy measure until day 30. The secondary analyses on primary endpoints were intended to be exploratory assessments that can be used to support the results from the primary endpoints. We enrolled patients in these two trials who were at least 18 years of age undergoing unilateral clear corneal cataract surgery. We excluded patients from these trials if, among other reasons, they had intraocular inflammation or ocular pain in the study eye at screening or had glaucoma or ocular hypertension.

We evaluated safety in all patients at each study visit with an assessment of general eye conditions, including visual acuity and IOP, along with any adverse events.

Efficacy: In the first Phase 3 clinical trial, DEXTENZA met the primary efficacy endpoint with statistical significance for the absence of cells in the anterior chamber compared to the vehicle control at day 14. 33.1% of DEXTENZA treated patients showed an absence of inflammatory cells in the anterior chamber of the study eye on day 14 following drug product insertion, compared to 14.5% of those receiving placebo vehicle control intracanalicular inserts ($p=0.0018$). DEXTENZA also met the primary efficacy endpoint with statistical significance for absence of pain compared to the vehicle control at day 8. 80.4% of patients receiving DEXTENZA reported absence of pain in the study eye on day 8 following insertion of the drug product, compared to 43.4% of those receiving placebo vehicle control intracanalicular inserts ($p< 0.0001$).

In the second Phase 3 clinical trial, DEXTENZA met the primary efficacy endpoint for absence of pain at day 8 with statistical significance but did not meet the primary efficacy endpoint for absence of inflammatory cells at day 14. In the second Phase 3 clinical trial, 77.5% of patients receiving DEXTENZA reported an absence of pain in the study eye on day 8 following insertion of the drug product, compared to 58.8% of those receiving placebo vehicle control intracanalicular inserts, a difference which was statistically significant ($p=0.0025$). However, 39.4% of DEXTENZA

treated patients showed an absence of inflammatory cells in the anterior chamber of the study eye on day 14 following drug product insertion, compared to 31.3% of those receiving placebo vehicle control intracanalicular inserts, a difference which was not statistically significant (p=0.2182).

In the third Phase 3 clinical trial, DEXTENZA met the primary efficacy endpoint with statistical significance for the absence of cells in the anterior chamber compared to the vehicle control at day 14. 52.1% of DEXTENZA treated patients showed an absence of inflammatory cells in the anterior chamber of the study eye on day 14 following drug product insertion compared to 31.2% of those receiving placebo vehicle control intracanalicular inserts (p< 0.0001). DEXTENZA also met the primary efficacy endpoint with statistical significance for absence of pain compared to the vehicle control at day 8. 79.3% of patients receiving DEXTENZA reported absence of pain in the study eye on day 8 following insertion of the drug product, compared to 61.3% of those receiving placebo vehicle control intracanalicular inserts (p< 0.0001).

Secondary analyses on primary endpoints for the three Phase 3 clinical trials were also completed. In the first Phase 3 clinical trial, statistically significant differences were seen for absence of pain at all time points (days 2, 4, 8, 14, 30 and 60) in the DEXTENZA treatment group compared to the vehicle control group. Statistically significant differences were seen for the absence of inflammatory cells at day 30 in the DEXTENZA treatment group compared to the vehicle control group, and there were no statistically significant differences seen at the other time points. Statistically significant differences between the DEXTENZA treatment group and the vehicle control group were seen for flare at days 8, 14 and 30.

In the second Phase 3 clinical trial, statistically significant differences were seen for absence of pain at days 2, 4, 14 and 30 in the DEXTENZA treatment group compared to the vehicle control group. A similar proportion of patients in the DEXTENZA treatment group and the vehicle control group were observed to have an absence of inflammatory cells at days 2, 4, 8, and 30. A statistically significant difference between treatment groups was not seen for the absence of inflammatory cells until the day 60 visit, at which time a greater proportion of patients in the DEXTENZA treatment group compared to the vehicle control group were observed to have an absence of inflammatory cells at day 60 (p=0.0012). Statistically significant differences between the DEXTENZA treatment group and the vehicle control group were seen for flare at days 14, 30 and 60.

In the third Phase 3 clinical trial, statistically significant differences were seen for absence of pain at all time points (days 2,4, 14, and 30) in the DEXTENZA treatment group compared to the vehicle control group. Statistically significant differences were seen for the absence of inflammatory cells at days 4, 8, and 30 but not seen at day 2. Statistically significant differences between the DEXTENZA treatment group and the vehicle control group were seen for flare at all measured time points (days 2, 4, 8, 14, and 30).

Safety: There were no ocular or treatment-related serious adverse events in the DEXTENZA treatment group in either of the first two completed Phase 3 clinical trials. There was one ocular serious adverse event in the vehicle control group in the first two completed Phase 3 clinical trials: hypopyon, or inflammatory cells in the anterior chamber. There were two patients with three serious adverse events in the DEXTENZA treatment group in the first Phase 3 clinical trial (1.2% incidence), compared with two patients with four serious adverse events in the vehicle control group (2.4% incidence). There were two serious adverse events in the DEXTENZA treatment group in the second Phase 3 clinical trial (1.3% incidence), compared with three serious adverse events in the vehicle control group (3.8% incidence). There were three serious adverse events in the DEXTENZA treatment group in the third Phase 3 clinical trial (1.4% incidence), compared with two serious adverse events in the vehicle control group (0.9% incidence). One serious adverse event in the DEXTENZA group was ocular in nature (retinal detachment). None of the serious adverse events in either group were deemed to be treatment-related.

Patients were randomized in a 2:1 ratio in the first two Phase 3 clinical trials and in a 1:1 ratio in the third Phase 3 clinical trial between the treatment group and the vehicle control group. In the first Phase 3 clinical trial, 98 adverse events were noted in the DEXTENZA group and 59 adverse events were noted in the vehicle control group. In the second Phase 3 clinical trial, 74 adverse events were noted in the DEXTENZA group and 47 adverse events were noted in the vehicle control group. In the third Phase 3 clinical trial, 91 adverse events were noted in the DEXTENZA group and 109 adverse events were noted in the vehicle control group. All adverse events were either resolved or considered chronic/stable at the time of subject exit from the study. We expect to be able to use the safety data from these Phase 3 trials to support our other DEXTENZA clinical development programs, including for allergic conjunctivitis.

Investigator-Initiated Trials

We have received proposals for, and plan to support, several investigator-initiated trials evaluating DEXTENZA in different clinical situations. To date, third-party clinical investigators have initiated over 25 trials to study the use of DEXTENZA in cataract surgery and other potential indications. Seven of the trials have completed enrollment, the remaining trials are actively enrolling and treated patients are being followed.

Regulatory Pathway

In November 2018, we received FDA approval for DEXTENZA for the pain indication. In January 2019, we submitted a sNDA for DEXTENZA for the treatment of post-surgical ocular inflammation. In June 2019, we received FDA approval for DEXTENZA for the inflammation indication. Although we conducted our Phase 3 clinical trials of DEXTENZA in patients who have undergone cataract surgery, these trials were intended to support, and DEXTENZA ultimately received, a label for patients who have undergone any ocular surgery.

Post-Approval Studies

In September 2020, we announced that we had dosed the first pediatric patients in a Phase 3 clinical trial evaluating DEXTENZA for the treatment of post-surgical ocular inflammation and pain in children following cataract surgery. This planned 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. The Phase 3 clinical trial is a U.S.-based, randomized, multicenter clinical trial in which we intend to enroll approximately 60 subjects. It is designed to evaluate the safety and biological activity 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 three years of age. The primary endpoint is the absence of pain at day eight post-treatment as measured by a FLACC (Face, Legs, Activity, Cry, Consolability) score of zero.

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 a 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 OTX-TIC, in specified Asian 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.

ReSure Sealant

ReSure Sealant is a topical liquid hydrogel that creates a temporary, adherent, soft and lubricious sealant to prevent post-surgical leakage from clear corneal incisions that are made during cataract surgery. The main components of ReSure hydrogel are water and PEG. ReSure hydrogel is completely synthetic, with no animal or human derived components. The FDA granted marketing approval for ReSure Sealant in January 2014. We commercially launched ReSure Sealant in the United States in February 2014.

ReSure Sealant provides a novel means of definitive wound closure in situations in which the surgeon observes a wound leak at the conclusion of surgery and/or would otherwise use sutures. We believe ReSure Sealant offers important benefits over sutures, including superior wound closure, a better safety profile and less follow-up.

The market opportunity for a surgical sealant following cataract surgery may be modest because sutures are used in a minority of cataract surgeries and, currently, there is no direct reimbursement for ReSure Sealant. While ReSure Sealant remains commercially available in the United States, there is no sales support and only limited commercial support for this product at this time. As a result, we do not expect to generate meaningful levels of revenue from the sale of ReSure Sealant.

Product Design

A surgeon forms ReSure Sealant hydrogel by combining three components: PEG, a cross-linker and a diluent buffer solution. The cross-linker interacts with the PEG molecules to form a molecular network that comprises the hydrogel. The components are mixed to initiate the cross-linking reaction to form a biocompatible, resorbable hydrogel. The hydrogel is approximately 90% water and is blue in color to help the surgeon visualize the sealant during application. The surgeon applies the sealant to the corneal incision as a liquid using a soft foam-tipped applicator. The sealant forms a conformal coating that adheres to the ocular tissue through mechanical interlocking of the hydrogel with the tissue surfaces. The blue color fades within a few hours following surgery. The soft, pliable hydrogel remains on the corneal surface during the critical wound healing period of one to three days and provides a barrier to fluid leakage. ReSure Sealant softens over time, detaches and is sloughed off in the tears as a liquid or extremely soft gel pieces. ReSure Sealant is designed to completely liquefy over a five to seven day duration. Complete epithelial healing takes place over this time period, providing long-term wound closure.

We provide ReSure Sealant in a sterile, single patient use package. The package contains a tray with two elongated mixing wells. Each well contains dried deposits of reactants, separated within the well. The package also contains one plastic dropper bottle filled with diluent solution and two applicators. The device is stored at room temperature for easy access.

ReSure Sealant Clinical Development

We conducted a pivotal clinical trial evaluating the safety and effectiveness of ReSure Sealant compared to sutures for preventing incision leakage from clear corneal incisions. In connection with FDA approval of ReSure Sealant in January 2014, we have agreed to conduct two post-approval studies. The first post-approval registry study was designed to confirm whether ReSure Sealant can be used safely by physicians in a standard cataract surgery practice and to confirm the incidence of pre-specified adverse ocular events in eyes treated with ReSure Sealant. The second post-approval study is designed to ascertain the incidence of endophthalmitis in patients treated with ReSure Sealant.

Pivotal Clinical Trial

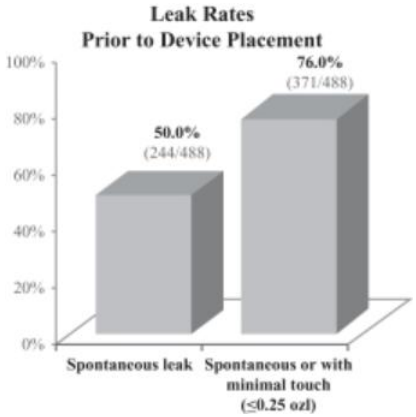
In 2013, we completed a prospective, randomized, parallel-arm, controlled, multicenter, subject-masked pivotal clinical trial evaluating the safety and effectiveness of ReSure Sealant. In this trial, we enrolled 488 patients at 24 sites across the United States. One patient was excluded prior to treatment because the surgeon was unable to achieve a dry ocular surface for application of ReSure Sealant. As a result, we randomized 304 patients for treatment with ReSure Sealant and 183 patients for treatment with sutures. Based on the trial protocol, 295 patients treated with ReSure Sealant and 176 patients treated with sutures completed study follow-up without a significant protocol deviation that directly affected the primary efficacy endpoint.

The primary efficacy endpoint was non-inferiority of ReSure Sealant to sutures for preventing incision leakage from clear corneal incisions within the first seven days following cataract surgery. A non-inferiority determination requires that the test product is not worse than the comparator by more than a small pre-specified margin. The non-inferiority margin for the ReSure Sealant pivotal clinical trial was a percentage difference in leak rates between ReSure Sealant and sutures of 5%.

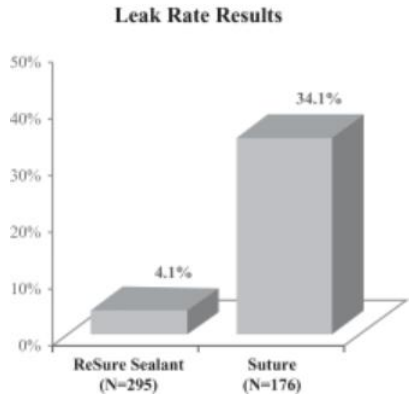
We randomized patients in a 5:3 ratio to receive either ReSure Sealant or sutures. All patients received a standardized self-sealing incision.

Surgeons assessed incision leakage during the operation and during follow-up visits on days 1, 3, 7 and 28 after the procedure. During the pre-randomization intraoperative evaluation, the surgeons assessed whether there was any leakage based on a standard test called a Seidel test in conjunction with an application of force near the incision using a standardized tool and technique. The surgeon slowly applied force using the standardized tool that we provided until a

leak was observed or until a pre-specified maximum force of one ounce of force was reached. In the assessments conducted during the operation, approximately 50% of leaks occurred spontaneously without application of force and 76% of leaks occurred with the application of 0.25 ounces of force or less.



Based on assessments conducted immediately following surgery, using the same standardized leak testing tool and technique, eyes receiving sutures leaked more frequently than eyes sealed with ReSure Sealant by a statistically significant margin of more than 8 to 1 ($p<0.0001$). In this trial, ReSure Sealant demonstrated both non-inferiority and superiority relative to the suture control based on the proportion of eyes with leakage within the first seven days after surgery. These results are shown in the figures below.



ReSure Sealant treated patients had significantly lower adverse event and device-related adverse event rates than patients treated with suture wound closure. We determined statistical significance based on a widely used, conventional statistical method that establishes the p-value of clinical results. Typically, a p-value of 0.05 or less represents statistical significance. In adverse events related to the study device, ReSure Sealant had a lower occurrence rate by a statistically significant margin of 1.6% for ReSure Sealant compared to 30.6% for sutures ($p<0.0001$). There were no significant or clinically relevant differences in the other safety endpoints, including slit lamp examination findings, between ReSure Sealant and suture patients, thus indicating that ReSure Sealant is well tolerated. Only one ReSure Sealant treated patient out of 299 (0.3%) had a wound healing assessment characterized as outside of normal limits at the day 7 assessment due to the presence of mild stromal edema. No ReSure Sealant treated subjects were outside of normal limits at the day 28 assessment. In this trial, surgeons rated ReSure Sealant as “easy” or “very easy” to use for 94.1% of patients treated with ReSure Sealant.

Post-Approval Studies

ReSure Sealant is classified in the United States as a class III medical device subject to the rules and regulation of premarket approval by the FDA. Following our submission of a PMA application to the FDA for review and during the

review process, the FDA completed compliance audits of our manufacturing facility and several of our pivotal clinical trial sites. Before granting approval of the PMA application, the FDA sought input from the Ophthalmic Devices Advisory Committee, a panel of physicians charged with reviewing results from our pivotal clinical trial. The FDA approved our PMA application for ReSure Sealant in January 2014.

The FDA required two post-approval studies as a condition for approval of our premarket approval, or PMA, application for ReSure Sealant. The first post-approval study, identified as the Clinical PAS, was to confirm that ReSure Sealant can be used safely by physicians in a standard cataract surgery practice and to confirm the incidence of the most prevalent adverse ocular events identified in our pivotal study in eyes treated with ReSure Sealant. We submitted the final study report to the FDA in June 2016 and the FDA has confirmed the Clinical PAS has been completed.

The second post-approval study, which we refer to as the Device Exposure Registry Study, was a retrospective analysis of the IRIS Registry, comparing endophthalmitis rates from sites that purchased ReSure Sealant versus those sites that did not. We completed the retrospective study in accordance with our agreement with the FDA and submitted the final study report for the Device Exposure Registry Study to the FDA in January 2021. We anticipate that the FDA will review the report within 90 days of our submission and notify us as to whether our obligation to conduct the post-approval study has been satisfied. Failure by us to conduct the required post-approval trial for ReSure Sealant to the FDA's satisfaction may result in withdrawal of the FDA's approval of ReSure Sealant or other regulatory action.

Foreign Approvals

Outside the United States, we plan to assess whether to seek regulatory approval for ReSure Sealant 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 do not currently plan to seek CE Mark approval to commercialize ReSure Sealant in the European Union. Outside of the United States and the European Union, we will need to engage a third party to assist us in the approval process. If we obtain regulatory approval to market and sell ReSure Sealant 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 ReSure Sealant. See "—Government Regulation—Review and Approval of Medical Devices in the European Union" for additional information.

Sales, Marketing and Distribution

We plan to prioritize our commercialization efforts in the United States. We generally expect to retain commercial rights in the United States to any of our local programmed-release drug delivery product candidates for front-of-the-eye diseases and conditions 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.

ReSure Sealant

We commercially launched ReSure Sealant in the United States in February 2014. While ReSure Sealant remains commercially available in the United States, there is no sales support and only modest commercial support for this product at this time. We may decide to actively promote ReSure Sealant in the future with the current sales force that supports DEXTENZA.

DEXTENZA

We sell DEXTENZA in the United States to a network of specialty distributors, who then resell DEXTENZA to ASCs and hospital outpatient departments, or HOPDs. In connection with our commercial launch of DEXTENZA, we have built a highly targeted, key account sales force that focuses on the ASCs responsible for the largest volumes of cataract surgery in the United States and their affiliates, with an initial emphasis on the approximately two million cataract procedures performed annually under Medicare Part B.

We expect to grow our salesforce in 2021 to increase our active number of accounts and penetrate each account more deeply. Our current field sales team consists of approximately 30 key account managers, or KAMs; nine Field Reimbursement Managers, or FRMs; and three Regional Directors, or RDs. We intend to add up to six KAMs and up to two FRMs, and we may add one RD, during the course of 2021.

We have entered into a license agreement and collaboration with AffaMed for the development and commercialization of DEXTENZA, along with OTX-TIC, in specified Asian markets.

If our sNDA to include the treatment of ocular itching associated with allergic conjunctivitis as an additional approved indication for DEXTENZA is approved, we expect to launch DEXTENZA for that indication in the first half of 2022. We expect initially to support the launch of DEXTENZA for this indication with our existing field force given the high degree of overlap between surgeons performing cataract surgery and those that treat severe allergic conjunctivitis. Following launch, we will consider the potential need for additional resources that may be required to support continued commercialization.

Manufacturing

We fabricate devices and drug products for use in our clinical trials, research and development and commercial efforts for all of our therapeutic product candidates using current Good Manufacturing Practices, or cGMP, at our facility located in Bedford, Massachusetts. In June 2016, we entered into a new lease agreement for approximately 71,000 square feet of a new facility in Bedford, Massachusetts that will include additional manufacturing space. We are evaluating the potential relocation of our manufacturing operations to the new leased premises. We plan to maintain our existing manufacturing space of approximately 20,000 square feet and extended the operating lease until June 2023.

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. Multiple vendors are available for each component we purchase. 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 front-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 process and prioritize 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 and ReSure Sealant 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 actively protect our innovations by seeking patents and other forms of intellectual property to cover our inventions. We also seek to in-license and acquire intellectual property to provide additional protection. As a result, we have 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.

Several patents and applications have been in-licensed from Incept. The license from Incept is limited to the fields of human ophthalmic diseases and conditions, acute post-surgical pain and ear, nose and/or throat diseases or conditions. As of February 26, 2021, we have licensed from Incept a total of 16 U.S. patents, 8 U.S. patent applications and foreign counterparts of some of these patents and patent applications.

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

OTX-TKI (axitinib intravitreal implant) for Wet AMD, DME and RVO

We have licenses to several U.S. patents and patent applications with the potential to cover this product candidate: three U.S. patents and issued patents in Australia, the European Union and Japan covering certain drug-release features of the hydrogel implant in combination with its hydrogel composition, all of which are expected to expire in 2027; two granted U.S. patents which are expected to expire in 2033 and 2034; and issued patents in Australia, Canada, China, Hong Kong, the European Union, India, Japan and South Korea covering the process of making the hydrogel implant with its drug release features and the resultant compositions that are expected to expire in 2032.

We own a pending patent application in the United States with the potential to cover this product candidate that, if granted, is expected to expire in 2041.

OTX-TIC (travoprost intracameral implant) for glaucoma or ocular hypertension

We have licenses to a pending U.S. application and foreign patent applications pending in Australia, Brazil, Canada, China, the European Union, Israel, India, Japan and Korea that potentially cover this product candidates that, if granted, are expected to expire in 2037.

We own a pending patent application in the United States and under the Patent Cooperation Treaty, or PCT, with the potential to cover this product candidate that, if granted, is expected to expire in 2042.

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

We have licenses to three U.S. patents, patents which have issued in Australia, Canada, China and Japan, and pending applications in the European Union and India that potentially cover this product candidate, all of which are expected to expire in 2030 and cover compositions and methods of use of this product candidate. We own a pending patent application in the United States with the potential to cover this product candidate that, if granted, is expected to expire in 2041.

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

We have licenses to three U.S. patents, patents which have issued in Australia, Canada, China and Japan, and pending applications in the European Union and India that potentially cover this product candidate, all of which are expected to expire in 2030 and cover compositions and methods of use of this product candidate. We own a pending patent application in the United States with the potential to cover this product candidate that, if granted, is expected to expire in 2041.

DEXTENZA ® (dexamethasone ophthalmic insert) 0.4 mg

We have licenses to three U.S. patents, patents which have issued in Australia, Canada, China and Japan, and pending applications in the European Union and India, that cover this product, all of which are expected to expire in 2030 and cover compositions and methods of use of this product candidate.

We also recently acquired a U.S. patent application with the potential to cover this product that, if granted, is expected to expire in 2036.

DEXTENZA ® (dexamethasone ophthalmic insert) 0.4 mg for allergic conjunctivitis

We have licenses to three U.S. patents, patents which have issued in Australia, Canada, China and Japan, and pending applications in the European Union and India, that potentially cover this product candidate, all of which are expected to expire in 2030 and cover compositions and methods of use of this product candidate. We own a pending patent application in the United States 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 covers the process of making and using hydrogel compositions. Our second U.S. patent is expected to expire in 2032 and covers certain features of the ReSure Sealant package.

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 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 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, we expect to apply for patent term extensions on 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.

For patent applications covering our products and developmental candidates, we typically file patent applications under the PCT which provides for the filing of a single application that preserves the right to file in national patent offices in other countries up to 30 months from the first priority date.

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, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data.

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 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 Agreement: (i) consistent with the Prior Agreement, a royalty equal to a low single-digit percentage of net sales by the 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 a license agreement, or the 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 OTX-TIC, or collectively with DEXTENZA, the AffaMed Licensed Products, regarding open-angle glaucoma and ocular hypertension, 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 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 License Agreement, we received upfront payments totaling $12 million in the fourth quarter of 2020. We are also eligible to receive up to an additional $91 million in aggregate, inclusive of a low-seven-figure clinical support payment, upon the achievement of certain development and commercial milestones. There can be no guarantee, however, that any of these 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 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 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 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 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. 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 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 us, at a prespecified premium. AffaMed has the right to terminate the License Agreement at any time following the completion of a Phase 3 clinical trial to evaluate OTX-TIC.

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 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 our Intracanalicular Insert Product Candidates

Several competitors are developing sustained drug release products for the same ophthalmic indications as our retinal implants, intracameral implants, intracanalicular insert and wound sealant products and product candidates, as set forth below.

Competitors of our Retinal Implants

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 one to two months or more of therapeutic effect. They include Lucentis, Eylea, Beovu 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 Clearside Biomedical, Inc., which is pursuing a TKI (axitinib) administered into the suprachoroidal space; Eyepoint Pharmaceuticals, Inc., which is pursuing a sustained-release bioerodible device containing a TKI (vorolanib) using its Durasert™ technology; Aerie Pharmaceuticals, which is

pursuing development of a 4-6 month TKI implant (axitinib) using its Print® manufacturing technology; Graybug Vision, Inc. which is pursuing a sustained-release microparticle depot TKI formulation (sunitinib) to extend therapeutic drug levels in ocular tissue for up to six months; and Kodiak Sciences Inc., which is pursuing sustained release therapies based on its anti-VEGF biopolymer conjugate technology. In addition, there are several companies pursuing gene therapy to treat retinal diseases including Adverum Biotechnologies, Inc. and REGENXBIO Inc. 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 including Apellis Pharmaceuticals, IVERIC bio, Inc., Annexion Biosciences, Gyroscope Therapeutics, Genentech/Ionis and Janssen Pharmaceutical, among others.

Competitors of OTX-TIC

Allergan PLC, now owned by AbbVie, Inc., 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 open-angle glaucoma or ocular hypertension. Allergan purchased ForSight VISION5 who was conducting a Phase 2 clinical development of the Helios insert, a sustained-release ocular insert placed below the eyelid that delivers bimatoprost for the treatment of glaucoma. Glaukos, Inc. is in Phase 3 trials with its iDose technology to deliver travoprost for the treatment of glaucoma. 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 development of an intracanalicular insert for the treatment of glaucoma.

Competitors of OTX-CSI and OTX-DED

A number of therapies are currently available for the treatment of DED in the United States. The most commonly used treatments for DED in the United States are over-the-counter eye drops, often referred to as “artificial tears,” and 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 DED. Kala Pharmaceuticals received approval in 2020 and launched EYESUVIS™, (loteprednol etabonate ophthalmic suspension) 0.25% for the short term (up to two weeks) treatment of the signs and symptoms of dry eye disease. 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 DED, including Aerie Pharmaceuticals, Alcon, Aldeyra Therapeutics, Allergan, Aurinia Pharmaceuticals, Azura Ophthalmics, Bausch Health (Novaliq), HanAll BioPharma, Johnson & Johnson, Mitotech, Novartis, Oyster Point Pharma, 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.

Competitors of ReSure Sealant

ReSure Sealant is the first and only surgical sealant approved for ophthalmic use in the United States. Outside the United States, Beaver Visitec is commercializing its product OcuSeal, which is designed to provide a protective hydrogel film barrier to stabilize ocular wounds. This product has received a CE Mark in Europe but is not approved for use in the United States. Sutures are the primary alternative for closing ophthalmic wounds. In addition, a technique called stromal hydration, which involves the localized injection of a balanced salt solution at the wound edges, is often used to facilitate the self-sealing of a wound.

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.

An applicant 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;
- 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 Good Clinical Practices, or GCP, 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, for a drug candidate product and a biological licensing application, or BLA, for a biological product requesting marketing 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. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. 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, applicants 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 determine whether human research subjects will be exposed to unreasonable health risks. 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. For our intracanalicular insert product candidates, we have typically conducted our initial and earlier-stage clinical trials outside the United States. We generally plan to conduct our later stage and pivotal clinical trials of our intracanalicular insert product candidates in the United States.

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. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Information about clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its ClinicalTrials.gov website.

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.

Drug and biologic companies are required to make publicly available their policies for expanded access for individual patient access to products intended for serious diseases. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study; or 15 days after the drug or biologic receives designation 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.

A sponsor may choose, but is not required, to conduct a foreign clinical trial under an IND. When a foreign clinical trial is conducted under an IND, all FDA 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 FDA requires such trials to be conducted in accordance with GCP, including review and approval by an independent ethics committee and informed consent from subjects. The GCP requirements encompass both ethical and data integrity standards for clinical trials. 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.

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.

Phase 3 clinical trials are commonly referred to as "pivotal" trials, which typically denotes a trial which presents the data that the FDA or other relevant regulatory agency will use to determine whether to approve a drug.

Progress reports detailing the safety results of the 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 case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Concurrent with clinical trials, companies often complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as 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 drug candidate and, among other things, must develop methods for testing the identity, strength, quality, purity, and potency of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

Pediatric Studies

Under the Pediatric Research Equity Act of 2003, an application or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug 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. With enactment of the Food and Drug Safety and Innovation Act, or the FDASIA, in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time. For drugs intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of an applicant, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments.

The FDA may, on its own initiative or at the request of the applicant, 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. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in the Food and Drug Administration Safety and Innovation Act, or FDASIA. The FDA maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population. Congress amended the FDA Reauthorization Act of 2017, or FDARA. Previously, drugs that had been granted orphan drug designation were exempt from the requirements of the Pediatric Research Equity Act. Under the amended section 505B, beginning on August 18, 2020, the submission of a pediatric assessment, waiver or deferral will be required for certain molecularly targeted cancer indications with the submission of an application or supplement to an application.

Review of an NDA or BLA by the FDA

In order to obtain approval to market a drug or biological product in the United States, a marketing application must be submitted to the FDA that provides data establishing the safety and effectiveness of the proposed drug product for the proposed indication, and the safety, purity and potency of the biological product for its intended indication. The application includes all relevant data available from pertinent preclinical and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, 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 effectiveness of the investigational drug product and the safety, purity and potency of the biological product to the satisfaction of the FDA.

The NDA and BLA are thus the vehicles through which applicants formally propose that the FDA approve a new product for marketing and sale in the United States for one or more indications. Every new product candidate must be the subject of an approved NDA or BLA before it may be commercialized in the United States. Under federal law, the submission of most applications is subject to an application user fee, which for federal fiscal year 2021 is $2,875,842 for an application requiring clinical data. The sponsor of an approved application is also subject to an annual program fee, which for fiscal year 2021 is $336,432. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for product candidates with orphan designation and a waiver for certain small businesses.

Following submission of an NDA or BLA, the FDA conducts a preliminary review of the application generally within 60 calendar days of its receipt and strives to inform the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept the 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. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs and BLAs. Under that agreement, 90% of applications seeking approval of New Molecular Entities, or NMEs, are meant to be reviewed within ten months from the date on which FDA accepts the application for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date. For applications seeking approval of products that are not NMEs, the ten-month and six-month review periods run from the date that FDA receives the application. The review process and the Prescription Drug User Fee Act goal date may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an application, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA or BLA submission, including drug component manufacturing (e.g., active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Under the FDA Reauthorization Act of 2017, the FDA must implement a protocol to expedite review of responses to inspection reports pertaining to certain applications, including applications for products in shortage or those for which approval is dependent on remediation of conditions identified in the inspection report.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity.

The FDA may refer an application for a novel product to an advisory committee or explain why such referral was not made. 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 recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

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.

The FDA's Decision on an Application

On the basis of the FDA's evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter, or CRL. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. 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. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the application, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the product candidate's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including 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-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval 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 Department of Health and Human Services, 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 addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, and its implementing regulations, as well as the Drug Supply Chain Security Act, or DSCA, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the federal level, and set minimum standards for the regulation of drug distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

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 applicant 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 applicant for approval of the application "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. 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) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant 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) applicant.

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

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute.

Specifically, in order for an abbreviated new drug application, or ANDA, to be approved, the FDA must find that the generic version is identical to the reference listed drug, or RLD, with respect to the active ingredients, the route of administration, the dosage form, and the strength 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 an 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. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA 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. An NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such exclusivity has been granted, an ANDA 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 applicant 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 applicant 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 a new dosage form, route of administration, combination or indication.

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 applicant 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 a new dosage form, route of administration, combination or indication. 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 seeking approval for generic versions of the drug as of the date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application to the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new 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 applicant does not challenge the listed patents or indicate that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

If the ANDA applicant or 505(b)(2) applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA 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 until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA applicant.

To the extent that the Section 505(b)(2) applicant is relying on trials conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. As a result, approval of a Section 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Biosimilars

The 2010 Patient Protection and Affordable Care Act, which was signed into law on March 23, 2010, or ACA, included a subtitle called the Biologics Price Competition and Innovation Act of 2009 or BPCIA. That Act established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. As of January 1, 2021, the FDA has approved 29 biosimilar products for use in the United States. No interchangeable biosimilars, however, have been approved. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars. Additional guidance is expected to be finalized by FDA in the near term.

Under the BPCIA, a manufacturer may submit an application for licensure of a biologic product that is "biosimilar to" or "interchangeable with" a previously approved biological product or "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 proposed biosimilar product in terms of safety, purity, and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and for products administered multiple times that the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date of approval of the reference product. The FDA may not approve a biosimilar product until 12 years from the date on which the reference product was approved. Even if a product is considered to be a reference product eligible for exclusivity, 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. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent exclusivity. 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 patent protection cover the product are extended by six months. This is not a patent term extension, but 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) applicant 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

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA 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. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The United States Patent and Trademark Office reviews and approves the application for any patent term extension or restoration 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 applicants and the agency. 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 2021, the standard fee is $365,657 and the small business fee is $91,414.

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

Certain products may be comprised of components that would normally be regulated under different types of regulatory authorities, and frequently by different Centers at the FDA. These products are known as combination products. Specifically, under regulations issued by the FDA, a combination product may be:

- a product comprised of two or more regulated components that are physically, chemically, or otherwise combined or mixed and produced as a single entity;
- two or more separate products packaged together in a single package or as a unit and comprised of drug and device products;
- a drug or device packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug or device where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the

approved product would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or

- any investigational drug or device 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.

Under the FDCA, the FDA is charged with assigning a center with primary jurisdiction, or a lead center, for review of a combination product. That determination is based on the "primary mode of action" of the combination product. Thus, if the primary mode of action of a device-drug combination product is attributable to the drug product, the FDA Center responsible for premarket review of the drug product would have primary jurisdiction for the combination product. The FDA has also established an Office of Combination Products to address issues surrounding combination products and provide more certainty to the regulatory review process. That office serves as a focal point for combination product issues for agency reviewers and industry. It is also responsible for developing guidance and regulations to clarify the regulation of combination products, and for assignment of the FDA center that has primary jurisdiction for review of combination products where the jurisdiction is unclear or in dispute.

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.

Clinical Trial Approval

Pursuant to the European Clinical Trials Directive, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of a European Union member state in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial after a competent ethics committee has issued a favorable opinion. Clinical trial application must be accompanied by an investigational medicinal product dossier with supporting information prescribed by the European Clinical Trials Directive and corresponding national laws of the member states and further detailed in applicable guidance documents.

In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. The new Clinical Trials Regulation will become directly applicable to and binding in all 28 EU Member States without the need for any national implementing legislation. It will overhaul the current system of approvals for clinical trials in the EU. Specifically, the new legislation aims at simplifying and streamlining the approval of clinical trials in the EU. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial will be required to submit a single application for approval of a clinical trial to a reporting EU Member State (RMS) through an EU Portal. The submission procedure will be the same irrespective of whether the clinical trial is to be conducted in a single EU Member State or in more than one EU Member State.

The Regulation was published on June 16, 2014 but has not yet become effective. In January 2020, the website of the European Commission reported that the implementation of the Clinical Trials Regulation was dependent on the development of a fully functional clinical trials portal and database, which would be confirmed by an independent audit, and that the new legislation would come into effect six months after the European Commission publishes a notice of this confirmation. The website indicated that the audit was expected to commence in December 2020. In late 2020, the EMA indicated that it plans to focus on the findings of a system audit; improving the usability, quality and stability of the clinical trial information system; and knowledge transfer to prepare users and their organizations for the new clinical trial system. The EMA has indicated that the system will go live in December 2021.

Marketing Authorization

To obtain marketing approval of a drug under European Union regulatory systems, an applicant 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 applicant 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 applicants 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 applicant, known as the reference member state. Under this procedure, an applicant 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.

Regulatory Data Protection in the European Union

In the EU, 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 applicants 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 EU 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.

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 EU 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 EU 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 EU 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 EU 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 EU'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 EU 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 EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU.

- 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 EU notably under Directive 2001/83EC, as amended, and EU Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the EU.

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 EU, medical devices must comply with the Essential Requirements in Annex I to the currently applicable EU 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 EU 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 will soon be 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 EU Medical Devices Directive. Unlike directives, which must be implemented into the national laws of the European Economic Area, or EEA, member states, the MDR will be directly applicable (i.e., without the need for adoption of EEA member State laws implementing them) in all EEA member states and are 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.

Currently, the MDR is scheduled to become applicable on May 26, 2021. Once applicable, the MDR 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 EU; 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

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the EU, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom left the EU on January 31, 2020. Under the withdrawal agreement, there is a transitional period until December 31, 2020 (extendable by up to two years). On December 24, 2020, the United Kingdom and the European Union entered into a Trade and Cooperation Agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction. Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the UK, as the UK legislation now has the potential to diverge from EU legislation. It remains to be seen how Brexit will impact regulatory requirements for product candidates and products in the UK in the long-term. The MHRA has recently published detailed guidance for industry and organizations to follow from January 1, 2021 now the transition period is over, which will be updated as the UK’s regulatory position on medicinal products evolves over time.

Furthermore, while the Data Protection Act of 2018 in the United Kingdom that “implements” and complements the European Union’s General Data Protection Regulation, or GDPR, has achieved Royal Assent on May 23, 2018 and is now effective in the United Kingdom, it is still unclear whether transfer of data from the European Economic Area, or EEA, to the United Kingdom will remain lawful under GDPR. The Trade and Cooperation Agreement provides for a transitional period during which the United Kingdom will be treated like an European Union member state in relation to processing and transfers of personal data for four months from January 1, 2021. This may be extended by two further months. After such period, the United Kingdom will be a “third country” under the GDPR unless the European Commission adopts an adequacy decision in respect of transfers of personal data to the United Kingdom. The United Kingdom has already determined that it considers all of the EU 27 and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the United Kingdom to the EU/EEA remain unaffected.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation, or 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, 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 also imposes strict rules on the transfer of personal data to countries outside the EU, 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 will be 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.

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 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.

We applied for a transitional pass-through reimbursement status on November 30, 2018 for DEXTENZA from CMS. In May 2019, we received formal notification from CMS that it had approved transitional pass-through payment status and established an interim billing code, known as a C-Code, for DEXTENZA that subsequently became effective on July 1, 2019. We also submitted an application to CMS for a J-Code for DEXTENZA in December 2018 and received a specific and permanent J-Code J1096 in July 2019 which became effective on October 1, 2019. With the effectiveness of our permanent J-Code for DEXTENZA as of October 1, 2019, our C-code is no longer in effect. J-Codes are familiar to both medical practices and their billing staffs, as well as Medicare (Part B and Part C) and commercial insurers. As a result, J-Codes generally allow for a simpler and more convenient reimbursement process. We expect pricing for DEXTENZA while in pass-through payment status to be approximately $538 per insert, and we expect pass-through status to remain in effect for up to three years from the effective date of the C-code, or July 1, 2019.

To date, four of seven Medicare Administrative Contractors, or MACs, have established physician fee schedules for the Category III Current Procedural Terminology, or CPT, procedure code 0356T currently in effect for the administration of drug-eluting intracanalicular inserts, including DEXTENZA: Novitas Solutions, Inc., or Novitas; First Coast Service Options, Inc., or First Coast; National Government Services, Inc., or NGS; and Wisconsin Physician Services, Inc, or WPS. The professional fee for CPT code 0356T is now eligible for physician payment for each insertion, in accordance with the applicable MAC's fee schedule. Novitas covers Medicare patients in New Mexico, Texas, Colorado, Oklahoma, Arkansas, Louisiana, Mississippi, New Jersey, Pennsylvania, Delaware, Virginia and the District of Columbia. First Coast covers Medicare patients in Florida, Puerto Rico, and the U.S. Virgin Islands. NGS covers Medicare patients in Illinois, Minnesota, Wisconsin, New York, Massachusetts, Connecticut, New Hampshire, Maine, Rhode Island, and Vermont. Wisconsin Physician Services, Inc. covers Medicare beneficiaries in Iowa, Kansas, Missouri, Nebraska, Indiana and Michigan. Combined, Novitas, First Coast, NGS and WPS cover over 60% of all Medicare beneficiaries. As of March 1, 2021, all seven MACs were reimbursing providers for intracanalicular insertions under CPT code 0356T despite only four of them having published physician fee schedules for the procedure.

On November 4, 2020, we announced that our application to the American Medical Association CPT Editorial Panel, or the Panel, for the creation of a Category I CPT procedure code had been granted. Category I CPT codes normally have a standardized Medicare physician fee schedule. As a result, they can improve coverage and payment across all payers for procedures performed in both the ASC and physician office settings. The Panel has agreed to create a permanent Category I CPT procedure code, effective January 1, 2022, to replace CPT code 0356T currently in effect for the administration of drug-eluting intracanalicular inserts including DEXTENZA.

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 Department of Health and Human Services information related to payments and other transfers of value to physicians 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.

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 United States 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 pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control 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, or ACA, which, among other things, includes changes to the coverage and payment for products under government health care programs.

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 2030 under the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act. 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 product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

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 Tax Cuts and Jobs Act of 2017, 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. Further, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the Court of Appeals for the Fifth Circuit affirmed the lower court's ruling that the individual mandate portion of the ACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. Thereafter, the U.S. Supreme Court agreed to hear this case. Oral argument in the case took place on November 10, 2020. On February 10, 2021, the Biden Administration withdrew DOJ's support for this lawsuit. A ruling by the U.S. Supreme Court is expected sometime this year. 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 rescinded those 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 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.

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States To date, 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 drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. To those ends, President Trump issued five executive orders intended to lower the costs of prescription drug products but it is unclear whether, and to what extent, these orders will remain in force under the Biden Administration. Further, on September 24, 2020, the Trump Administration finalized a rulemaking allowing states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

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 health care authorities 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 health care 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, 2020, we had 181 full-time employees. The following table provides an overview of the distribution of those employees:

Department	Headcount
Research & Development	73
Sales & Marketing	67
Manufacturing	13
General & Administrative	28
Total Employees	181

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. As of December 31, 2020, our workforce was composed of 48% female and 52% male, and 25% of the workforce was non-white.

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 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. In response to the COVID-19 pandemic, we have implemented significant changes that we determined were in the best interest of our employees, as well as the communities in which we operate, and which comply with government regulations. This includes allowing a number of our corporate employees to work remotely, as appropriate, while implementing significant safety measures designed to protect the health of all those entering our office.

Our Corporate Information

We were incorporated under the laws of the State of Delaware in 2006. Our principal executive offices are located at 24 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 page 1 of this Annual Report on Form 10-K for a discussion of some of the forward-looking statements that are qualified by these risk factors and the summary of principal risks facing our business that follows. 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 the Coronavirus Pandemic

The coronavirus (COVID-19) pandemic has disrupted, and is expected to continue to adversely affect, our operations, including the progress of our commercialization of DEXTENZA and our ability to generate revenue from sales of DEXTENZA or ReSure Sealant. In the future, it may have other adverse effects on our business and operations, including potentially delaying one or more of our clinical trials. In addition, this pandemic initially caused substantial disruption in the financial markets and has adversely impacted economies worldwide, both of which could result in adverse effects on our business, operations and ability to raise capital.

The COVID-19 coronavirus pandemic, which began in December 2019 and has spread worldwide, has caused many governments to implement measures to slow the spread of the outbreak through quarantines, strict travel restrictions, heightened border scrutiny, and other measures. The outbreak and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. The future progression of the pandemic and its effects on our business and operations are uncertain.

We believe the COVID-19 pandemic has adversely affected, and we expect it to continue to adversely affect, the progress of our commercialization of DEXTENZA and our ability to generate revenue from sales of DEXTENZA, as a result of many factors, including:

- a decrease in patients attending routine ophthalmology appointments or undergoing elective surgical procedures, including cataract surgery;
- diversion of healthcare resources away from elective surgical procedures, including cataract surgery, to focus on pandemic concerns;
- potential interruptions in global shipping affecting the transport of raw materials used in the manufacture of our product, drug product, patient samples and related literature; and
- the prolonged impact on travel that might continue to interrupt key commercialization activities, such as travel by our key account managers, which could adversely impact the progress of our commercialization of DEXTENZA.

The COVID-19 pandemic also has the potential to delay or otherwise adversely affect our clinical development activities, including our ability to recruit or retain patients in our ongoing clinical trials, as a result of many factors, including:

- diversion of healthcare resources away from the conduct of our clinical trials to focus on pandemic concerns, including the availability of necessary materials, the attention of physicians serving as our clinical trial investigators, access to hospitals serving as our clinical trial sites, and availability of hospital staff supporting the conduct of our clinical trials;
- the inability or reluctance of patients enrolled in our clinical trials to visit clinical trial sites if patients are affected by the virus or are fearful of traveling to our clinical trial sites because of the outbreak;

- potential interruptions in global shipping affecting the transport of clinical trial materials, such as investigational drug product, patient samples, and raw materials used in the manufacture of our product candidates; medical and laboratory supplies used in our clinical trials or preclinical studies; or animals that are used for preclinical testing, and other supplies used in our clinical trials and preclinical studies;

- the impact of personnel shortages, further limitations on travel, or other operational challenges that could interrupt key clinical trial activities, such as clinical trial site initiations and monitoring and reporting activities, travel by our employees, contract research organizations, or CROs, or patients to clinical trial sites, or the ability of employees at our manufacturing facility to report to work, any of which could delay or adversely impact the conduct or progress of our clinical trials or limit the amount of clinical data we will be able to report; and

- any future interruption of, or delays in receiving, supplies of clinical trial material from our manufacturing facility due to stay-at-home orders, production slowdowns or stoppages, or disruptions in delivery systems.

Any negative impact that the COVID-19 pandemic has on recruiting or retaining patients in our clinical trials, the ability to provide materials for our product candidates, the operations of our clinical trials, or the regulatory review process could cause additional delays with respect to product development activities, which could materially and adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses, affect our ability to raise additional capital, and have a material adverse effect on our financial results. For example, we saw a slight slowdown in our enrollment in the fourth cohort of our Phase 1 clinical trial evaluating OTX-TIC due to COVID-19. As a result, we provided topline data for this clinical trial in the first quarter of 2021 instead of the fourth quarter of 2020 as originally planned. If similar delays affect our enrollment of our planned Phase 2 clinical trial for OTX-TIC or any of our ongoing or planned clinical trials, the completion of such trials could be delayed.

Additionally, in May 2020, we disclosed the receipt of interim data regarding our ongoing Phase 1 clinical trial of OTX-TKI for the potential treatment of wet AMD and other retinal diseases. The Phase 1 clinical trial is a multi-center, open-label, dose-escalation study in Australia designed to evaluate the safety, biological activity, durability and tolerability of OTX-TKI. At that time, two cohorts had been enrolled, a lower dose cohort of 200 µg and a higher dose cohort of 400 µg. We disclosed that, as of May 13, 2020, the first two patients in the second (400 µg) cohort had shown a clinically meaningful reduction in intraretinal and/or subretinal fluid out to six months with a single implant. In July 2020, we reported that the data collection and other administrative activities of the clinical trial site in Australia where these two patients were being treated had been adversely impacted by the effects of the COVID-19 pandemic. Specifically, the clinical trial site reported to us that one of these two patients showing a clinically meaningful reduction in intraretinal and/or subretinal fluid had been treated with anti-VEGF medication at a site visit at month 4.5 (in mid-March 2020) and at month 6 (in early May 2020). The administration of this anti-VEGF medication at the month 4.5 visit and at the month 6 visit was not entered into the clinical trial database until after a subsequent visit at month 7.5 in mid-June 2020. As a result, this information was not available to or known by us in connection with our prior disclosures.

The COVID-19 pandemic continues to evolve and its ultimate scope, duration and effects are unknown. The extent of the impact on our business, preclinical studies and clinical trials, commercialization activities and revenue will depend on future developments, which are highly uncertain and cannot be predicted with confidence. These include, but are not limited to, the duration of the outbreak; actions to contain the pandemic or treat its impact, such as travel restrictions, vaccination campaigns, social distancing and quarantines or lock-downs in the United States and other countries; business closures or business disruptions; and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

The pandemic initially caused significant disruptions in the financial markets, and may cause additional disruptions in the future, any of which could adversely impact our ability to raise additional funds through public offerings or private placements or impact the volatility of our stock price and trading in our stock. Moreover, the pandemic has significantly impacted economies worldwide, which could result in adverse effects on our business and operations. We cannot be certain what the overall impact of the COVID-19 pandemic will be on our business and it has the potential to continue to adversely affect our business, financial condition, results of operations, and prospects.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net losses were $60.0 million for the year ended December 31, 2018, $86.4 million for the year ended December 31, 2019 and $155.6 million for the year ended December 31, 2020. As of December 31, 2020, we had an accumulated deficit of $539.3 million. We have financed our operations primarily through private placements of our preferred stock, public offerings of our common stock, private placements of our convertible notes and borrowings under credit facilities. 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 ReSure Sealant and DEXTENZA® for the treatment of ocular inflammation and pain following ophthalmic surgery. Although we expect to continue to generate revenue from sales of ReSure Sealant and 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 to commercialize DEXTENZA in the United States;
- continue to develop and expand our sales, marketing and distribution capabilities for DEXTENZA and any of our products or product candidates;
- continue to pursue the clinical development of DEXTENZA for additional indications;
- continue ongoing clinical trials of our product candidates OTX-TKI, OTX-TIC, OTX-CSI, and OTX-DED;
- initiate planned Phase 2 clinical trials for our product candidates OTX-TKI and OTX-TIC;
- conduct joint research and development under our strategic collaboration with Regeneron, for the development and potential commercialization of products containing our extended-delivery hydrogel formulation in combination with Regeneron’s large molecule, VEGF-targeting compounds to treat retinal diseases;
- conduct research and development activities on, and seek regulatory approvals for, DEXTENZA and OTX-TIC in certain Asian countries 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, including through additional preclinical development activities associated with our front-of-the-eye and back-of-the-eye programs and potential opportunities outside the field of ophthalmology;
- 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, our ongoing 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 and management systems and personnel, including personnel to support our clinical development, manufacturing and commercialization efforts and our operations as a public company;
- defend ourselves against legal proceedings;
- 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 expenses will increase if:

- we are required by the FDA or the European Medicines Agency, or EMA, 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; or
- there are any delays in enrollment of patients in or completing our clinical trials or the development of our product candidates.

Prior to our commercial launch of DEXTENZA in July 2019, ReSure Sealant was our only source of revenue from product sales. However, sales of ReSure Sealant have not generated, and we do not anticipate that they will ever generate, significant revenue. 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:

- successfully continuing to commercialize DEXTENZA in the United States, including by further developing our sales force, marketing and distribution capabilities;
- successfully completing clinical development of our product candidates, including DEXTENZA for additional indications as well as OTX-TKI, OTX-TIC, OTX-CSI, and OTX-DED;
- obtaining marketing approval for these product candidates;
- manufacturing at commercial scale, marketing, selling and distributing DEXTENZA and 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 third-party payors for our products; and
- protecting our rights to our intellectual property portfolio.

Our ability to generate revenue from operations will depend, in part, on the timing and success of commercial sales of DEXTENZA. However, the successful commercialization of DEXTENZA in the United States is subject to many risks. The COVID-19 pandemic has reduced the number of elective ophthalmic surgeries performed since mid-March 2020. Although we saw signs of a partial recovery in the number of cataract surgeries during the second half of 2020, we believe the number of procedures currently being performed continues to be below the level performed prior to the COVID-19 pandemic. DEXTENZA is our first significant product launch, and we may not be able to continue to commercialize DEXTENZA successfully. There are numerous examples of unsuccessful product launches and failures to meet expectations of market potential, including by pharmaceutical companies with more experience and resources than we have. We do not anticipate revenue from sales of DEXTENZA for the treatment of ocular inflammation and pain following ophthalmic surgery will be sufficient for us to become profitable for several years, if ever. Furthermore,

if we are unable to achieve our revenue estimates for DEXTENZA, our ability to raise additional capital may be negatively impacted.

We may not succeed in our continued commercialization efforts and may never generate revenue that is sufficient to achieve profitability. 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 company 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, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect to devote substantial financial resources to our ongoing and planned activities, particularly as we continue to commercialize DEXTENZA for the treatment of ocular inflammation and pain following ophthalmic surgery and any additional indications for which we receive marketing approval, including expanding our product manufacturing, sales, marketing and distribution capabilities, and advance OTX-TKI, OTX-TIC, OTX-CSI, and OTX-DED through Phase 2 clinical development. We also expect to devote substantial financial resources as we conduct late stage clinical trials for our local programmed-release drug delivery product candidates, including DEXTENZA for additional indications including ocular itching associated with allergic conjunctivitis, and seek marketing approval for any such product candidate for which we obtain favorable pivotal clinical results. In addition, we plan to devote significant financial resources to conducting research and development and potentially seeking regulatory approval for our other product candidates. Accordingly, we will need to obtain substantial additional funding to fully support our continuing operations and ongoing commercialization efforts for DEXTENZA. 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 any future commercialization efforts.

As of December 31, 2020, we had cash and cash equivalents of $228.1 million, outstanding debt of $25.0 million, net of unamortized discount, and $37.5 million aggregate principal amount of senior subordinated convertible notes plus accrued interest of $4.2 million. We believe that our existing cash and cash equivalents of $228.1 million as of December 31, 2020, will enable us to fund our planned operating expenses, debt service obligations and capital expenditure requirements through 2023. This estimate is based on our current operating plan which includes estimates of anticipated cash inflows from DEXTENZA and ReSure Sealant product sales and cash outflows from operating expenses. These estimates are subject to various assumptions including those related to the severity and duration of the COVID-19 pandemic, the revenues and expenses associated with the commercialization of DEXTENZA, variable expense reductions, the pace of our research and clinical development programs, and other aspects of our business. We have based our estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect and would therefore need to raise additional capital to support our ongoing operations or adjust our plans accordingly. Our future capital requirements will depend on many factors, including:

- our ability to continue to commercialize and sell DEXTENZA in the United States;
- the costs, timing and outcome of regulatory review of our product candidates by the FDA, the EMA or other regulatory authorities;
- the level of product sales from DEXTENZA and any additional products for which we obtain marketing approval in the future;
- the costs of manufacturing, sales, marketing, distribution and other commercialization efforts with respect to DEXTENZA and any additional products for which we obtain marketing approval in the future;
- the costs of expanding our facilities to accommodate our manufacturing needs and headcount;
- the progress, costs and outcome of our planned and ongoing clinical trials of our extended-delivery drug delivery product candidates, in particular DEXTENZA for additional indications, OTX-TIC for the treatment of glaucoma or ocular hypertension, OTX-TKI for the treatment of wet AMD, 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;

- the scope, progress, costs and outcome of preclinical development and clinical trials of our other product candidates;
- 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, from Regeneron as potential option exercise fees, development, regulatory and sales milestone payments and royalty payments and the amounts we are obligated to pay to Regeneron as reimbursement if it chooses to exercise its option to advance a product candidate under our collaboration agreement;
- the amounts we are entitled to receive, if any, from AffaMed 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 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 achieve profitability. We may not generate significant revenue from sales of any product for several years, if at all. 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. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

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 collaboration agreement with Regeneron provides for Regeneron's reimbursement of certain preclinical expenses incurred by us under our collaboration agreement and for the potential receipt of option exercise, development, regulatory and sales milestone and royalty payments and 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 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. Our pledge of our assets as collateral to secure our obligations under our credit facility pursuant to which we have a total borrowing capacity of $25.0 million, which has been fully drawn down, or the Credit Facility may limit our ability to obtain additional debt financing. If we are unable to raise additional funds through equity or debt financings 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. The COVID-19 pandemic initially caused significant disruptions in the financial markets, and may cause disruptions in the future, any of which could adversely impact our ability to raise additional funds through equity or debt financings.

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.

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

We have a significant amount of indebtedness. Under our Credit Facility, as amended to date, we have $25.0 million, net of unamortized discount, of outstanding principal indebtedness. Under the accompanying credit and security agreement, as amended and/or restated to date, the Credit Agreement, we were permitted to make interest-only payments until January 1, 2021. Our obligations under the Credit Agreement are secured by all of our assets, including our intellectual property. The Credit Agreement also includes customary affirmative and negative covenants, including limitations on dispositions, mergers or acquisitions; incurring indebtedness, liens or encumbrances; paying dividends; making certain investments; and engaging in certain other business transactions. In March 2019, we issued $37.5 million aggregate principal amount of issued and outstanding senior unsubordinated convertible notes, or the Convertible Notes. The Convertible Notes mature on March 1, 2026 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 our 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, which would reduce the amounts available to fund working capital, commercialization expenditures associated with DEXTENZA, capital expenditures, product development efforts and other general corporate purposes;

- obligating us to negative covenants restricting our activities, including limitations on dispositions, mergers or acquisitions, encumbering our intellectual property, incurring additional indebtedness or liens, paying dividends, making investments and engaging in certain other business transactions;

- 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. In addition, a failure to comply with the conditions of our Credit Agreement or the Convertible Notes could result in an event of default under those instruments. In the event of an acceleration of amounts due under our Credit Agreement or the Convertible Notes as a result of 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, operations, properties, assets or condition or a failure to pay any amount due, 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. In addition, the covenants under our existing Credit Agreement and the pledge of our assets, including our intellectual property, as collateral limit our ability to obtain additional debt financing.

The elimination of LIBOR could adversely affect our business, results of operations or financial condition.

In July 2017, the head of the United Kingdom Financial Conduct Authority, or FCA, announced plans to phase out the use of LIBOR by the end of 2021. In November 2020, the International Exchange Benchmark Administration, the administrator of LIBOR, announced its decision to consult on ceasing the publication of rates for certain short-term LIBOR tenors effective December 31, 2021, and for the remaining tenors effective June 30, 2023. Financial regulatory agencies including the U.S. Federal Reserve and the FCA expressed support for announcement. Although the impact is uncertain at this time, the elimination of LIBOR could have an adverse impact on our business, results of operations, or financial condition. We may incur significant expenses to amend our LIBOR-indexed loans and other applicable financial or contractual obligations, including our Credit Facility, to a new reference rate, which may differ significantly from LIBOR. Accordingly, the use of an alternative rate could result in increased costs, including increased interest expense on our credit facilities, and increased borrowing and hedging costs in the future. At this time, no consensus exists as to what rate or rates may become acceptable alternatives to LIBOR and we are unable to predict the effect of any such alternatives on our business, results of operations or financial condition.

Our limited operating history may make it difficult for our stockholders to evaluate the success of our business to date and to assess our future viability.

We are an early-stage company. Our operations to date have been limited to organizing and staffing our company, acquiring rights to intellectual property, business planning, raising capital, developing our technology, identifying potential product candidates, undertaking preclinical studies and clinical trials, manufacturing initial quantities of our products and product candidates, and commercializing ReSure Sealant and DEXTENZA for the treatment of ocular inflammation and pain following ophthalmic surgery. We have a limited history of commercializing products. To date, we have not generated significant revenue from the sale of either ReSure Sealant or DEXTENZA or revenue that is sufficient to achieve profitability. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We are in early stages of the process of transitioning from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter-to-quarter and year-to-year due to a variety of factors, many of which are beyond our control. Accordingly, our stockholders should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

We have broad discretion in the use of our available cash and other sources of funding and may not use them effectively.

Our management has broad discretion in the use of our available cash and other sources of funding and could spend those resources in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could cause the price of our common stock to decline and delay the development of our product candidates. Pending its use, our available cash may be invested in a manner that does not produce income or that loses value.

Risks Related to Product Development

We depend heavily on the success of DEXTENZA and our product candidates. Clinical trials of our product candidates may not be successful. If we are unable to successfully complete clinical development of and obtain marketing approvals for our product candidates, or experience significant delays in doing so, or if after obtaining marketing approvals, we fail to maintain marketing approval or fail to commercialize these product candidates, our business will be materially harmed.

We have devoted a significant portion of our financial resources and business efforts to the development of our drug-eluting intracanalicular insert products for diseases and conditions of the front of the eye and for our other product candidates. In particular, we are investing substantial resources to complete the development of DEXTENZA for

allergic conjunctivitis, OTX-TKI for wet AMD, OTX-TIC for glaucoma or ocular hypertension, 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 have received a target action date under the Prescription Drug User Fee Act, commonly known as PDUFA, of October 18, 2021, for our supplemental New Drug Application, or sNDA, to include ocular itching associated with allergic conjunctivitis as an additional indication. We currently have several ongoing and planned clinical trials, including our Phase 1 clinical trial of OTX-TKI, our Phase 1 clinical trial of OTX-TIC, our Phase 2 clinical trial of OTX-CSI, and our Phase 2 clinical trial for OTX-DED. If these or other 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 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 products and 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 commercialization of DEXTENZA for the treatment of ocular inflammation and pain following ophthalmic surgery and our obtaining marketing approval for and commercializing other products with significant market potential, including DEXTENZA for additional indications.

The commercial success of our product DEXTENZA and our product candidates 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 for our product candidates;
- scaling up our manufacturing processes and capabilities to support additional or larger clinical trials of our product candidates and commercialization of DEXTENZA or any of our product candidates for which we obtain marketing approval;
- 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 and product candidates, if and when approved, whether alone or in collaboration with others;
- partnering successfully with our current and future collaborators, including Regeneron and AffaMed;
- gaining acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- maintaining a continued acceptable safety profile of our products following approval;
- obtaining and maintaining coverage and adequate reimbursement from third-party payors;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity; and
- protecting our rights in our intellectual property portfolio.

In certain cases, such as in our collaborations with Regeneron and AffaMed, many of these factors may be 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.

If clinical trials of our intracanalicular insert, intravitreal implant, intracameral implant, or suprachoroidal implant product candidates or any other product candidate that we develop fail to demonstrate safety and efficacy to the satisfaction of the FDA, the EMA 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.

Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, including our intracanalicular insert product candidates, 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. 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.

In general, the FDA requires two adequate and well-controlled clinical trials to support the effectiveness of a new drug for marketing approval. In a Phase 2 clinical trial of DEXTENZA that we completed in 2013 in which we were evaluating DEXTENZA for post-surgical ocular inflammation and pain following cataract surgery, DEXTENZA did not meet the primary efficacy endpoint for inflammation with statistical significance at the pre-specified time point at day 8. However, we did achieve statistical significance for this inflammation endpoint at days 14 and 30. Accordingly, we measured the primary efficacy endpoint for inflammation in our completed Phase 3 clinical trials of DEXTENZA at day 14. In the first and third Phase 3 clinical trials, DEXTENZA met both primary endpoints for post-surgical ocular inflammation and pain following cataract surgery with statistical significance. However, in the second Phase 3 clinical trial, DEXTENZA met only one of the two primary efficacy endpoints with statistical significance. In this second trial, DEXTENZA did not meet the primary endpoint relating to absence of inflammatory cells in the study eye at day 14.

We announced topline results from a third Phase 3 clinical trial of DEXTENZA for post-surgical ocular inflammation and pain in November 2016, which we used to support the potential labeling expansion of DEXTENZA's indications for use. We modified the design of this third Phase 3 clinical trial compared to our two previous Phase 3 clinical trials of DEXTENZA based on our learnings from these trials. In this trial, DEXTENZA successfully met its two primary efficacy endpoints for inflammation and pain, achieving statistically significant differences between the treatment group and the placebo group for the absence of inflammatory cells on day 14 and the absence of pain on day 8, respectively. Secondary analyses on the primary efficacy measures have also been completed. DEXTENZA achieved each of the secondary endpoints related to absence of inflammatory cells, absence of pain, and absence of anterior chamber flare with statistical significance compared to placebo at each of the pre-specified time points, with the exception of the endpoint for the absence of inflammatory cells at day 2 (which is the day following surgery). Based on the results of our third Phase 3 clinical trial of DEXTENZA and subsequent approval in November 2018 for the pain indication pursuant to the initial NDA, we submitted an sNDA for DEXTENZA for the treatment of post-surgical ocular inflammation in January 2019, and the FDA approved the sNDA in June 2019.

In our first Phase 3 clinical trial of DEXTENZA for allergic conjunctivitis, for which we announced topline results in October 2015, DEXTENZA met one of the two primary endpoints. DEXTENZA achieved the primary endpoint for ocular itching associated with allergic conjunctivitis but not the primary endpoint for conjunctival redness, in each case measured on day 7 after insertion of the insert. The difference in the mean scores for ocular itching between the DEXTENZA group and the placebo group was greater than 0.5 units on a five point scale at all time points on day 7 post-insertion and was greater than 1.0 unit at a majority of the time points on day 7 post-insertion. The DEXTENZA group did not achieve these pre-specified endpoints on day 7 post-insertion with respect to conjunctival redness. In our second Phase 3 clinical trial of DEXTENZA for allergic conjunctivitis, for which we announced topline results in June 2016, DEXTENZA did not meet the sole primary endpoint for ocular itching. The single primary endpoint of the second Phase 3 clinical trial was the difference in the mean scores in ocular itching between the treatment group and the placebo comparator group at three time points on day 7 following insertion of the inserts. While mean ocular itching was seen to be numerically lower (more favorable) in the DEXTENZA treatment group compared to the placebo group measured at each of the three specified times on day 7 following insertion of the inserts, at 3, 5, and 7 minutes by -0.18, -0.29, and -

0.29 units, respectively, on a five point scale, this difference did not reach statistical significance. In addition, the trial did not achieve the requirement of at least a 0.5 unit difference at all three time points on day 7 following insertion of the inserts and at least a 1.0 unit difference at the majority of the three time points between the treatment group and the placebo group on day 7 following insertion of the inserts. Further, in our prior Phase 2 clinical trial of DEXTENZA in which we were evaluating DEXTENZA for allergic conjunctivitis, DEXTENZA met one of the two primary efficacy measures. The DEXTENZA treatment group achieved a mean difference compared to the vehicle control group of more than 0.5 units on a five point scale on day 14 for all three time points measured in a day for both ocular itching and conjunctival redness. The DEXTENZA group did not achieve a mean difference compared to the vehicle control group of 1.0 unit for the majority of the three time points measured on day 14 for either ocular itching or conjunctival redness. Post-hoc analyses that we performed on the results of our two completed Phase 3 clinical trials for allergic conjunctivitis may not be predictive of success in any future Phase 3 clinical trial. Although we believe that these analyses provide important information regarding DEXTENZA and are helpful in understanding the results of this trial and determining the appropriate criteria for future clinical trials, post-hoc analyses performed using an unlocked clinical trial database can result in the introduction of bias and are given less weight by regulatory authorities than pre-specified analyses.

Even if we obtain favorable clinical trial results in an additional Phase 3 clinical trial of DEXTENZA for allergic conjunctivitis, such as our third Phase 3 clinical trial, including meeting all primary efficacy measures, we may not obtain approval for DEXTENZA to treat allergic conjunctivitis or ocular itching associated with allergic conjunctivitis, or the FDA may require that we conduct additional clinical trials. For example, in April 2020, we announced the topline results from our third Phase 3 clinical trial assessing ocular itching associated with allergic conjunctivitis in which DEXTENZA achieved its primary endpoint as treated subjects demonstrated a statistically significant (p-value < 0.0001) difference in mean ocular itching scores compared to vehicle-treated subjects at all three pre-specified time points compared with placebo-treated subjects. We believe that this efficacy data, considered in totality with a favorable safety profile and the data from the prior Phase 2, Phase 3a and Phase 3b clinical trials, provides the basis for a submission of an sNDA for DEXTENZA to include the treatment of ocular itching associated with allergic conjunctivitis as an additional approved indication. However, the FDA may not agree with our view of the clinical meaningfulness of the data. We understand that the FDA has in the past considered, for trials similar to ours, clinical meaningfulness to be a 0.5 unit difference at all relevant time points and at least a 1.0 unit difference at a majority of time points assessed. DEXTENZA did not achieve these measures in the third Phase 3 clinical trial. Achievement of such differences is also affected by the statistical methodology we utilize to review the clinical trial data. As previously disclosed, in our first Phase 3 clinical trial for the treatment of ocular itching associated with allergic conjunctivitis, DEXTENZA achieved a 0.5 unit difference at all relevant time points and at least a 1.0 unit difference at a majority of time points assessed using the Markov Chain Monte Carlo, or MCMC, method where the basis for imputation was at the individual eye level. However, using the MCMC method specified in the applicable statistical analysis plan—where the basis for imputation is at the subject level (average of the two eyes)—DEXTENZA did not achieve all of these measures. If the FDA were to require that a product candidate achieve these measures of clinical meaningfulness, approval of our sNDA could be delayed or prevented.

From time to time, we may decide to conduct clinical trials to assess patients' 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 glaucoma and ocular hypertension. 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 success of our intracanalicular insert product candidates is dependent upon retention during the course of intended therapy. As such, we may conduct non-significant risk investigational device exemption, or IDE, medical device, or NSR, studies in the United States for our extended-delivery intracanalicular insert in an effort to increase the rate of retention. All NSR studies that we have performed to date have involved placebo vehicle control intracanalicular inserts without active drug. If we determine to make any future changes to the design or composition of our inserts, such changes could affect the outcome of any subsequent clinical trials using these updated inserts. For example, in our Phase 2b clinical trial of OTX-TP, we used a different version of intracanalicular insert than either of the inserts that we used in our Phase 2a clinical trial of OTX-TP. Based on the results of our completed Phase 2a clinical trial, we designed the OTX-TP insert that was used in our Phase 2b clinical trial to deliver drug over a 90 day period at the same daily rate as the two-month version of the insert used in the Phase 2a clinical trial. To achieve this, we modified the design of the

OTX-TP insert to enlarge it in order to enable the insert to carry a greater amount of drug. In addition, we incorporated minor structural changes to improve retention rates. In our Phase 2b clinical trials, OTX-TP inserts could be visualized in approximately 88% of eyes by the day 60 visit. By the day 90 visit, the ability to visualize OTX-TP had declined to approximately 42% of eyes as the hydrogel softened, liquefied and had either advanced further down in the canaliculus or had cleared through the nasolacrimal duct.

We are conducting additional NSR studies on additional modified insert designs, including a polyethylene glycol, or PEG, tip on the proximal end of the insert that have been incorporated into the design of certain of our clinical trials. If the retention rates for our inserts in future clinical trials are inadequate to ensure that the patient is receiving appropriate therapy, we may not be able to obtain regulatory approvals or, even if approved, achieve market acceptance of our local programmed-release drug delivery 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. For certain of our product candidates, we have chosen to conduct our initial or earlier-stage clinical trials outside the United States. We generally plan to conduct our later stage and pivotal clinical trials of our product candidates in the United States. The FDA, however, could require us to conduct additional studies or require us to modify our planned pivotal clinical trials to receive clearance to initiate such trials in the United States or to continue such trials once initiated. 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.

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 have often conducted our initial and earlier-stage clinical trials for our product candidates outside the United States. We are currently conducting a Phase 1 clinical trial for our product candidate OTX-TKI for the treatment of wet AMD in Australia, and pending our receipt and review of topline data in the Phase 1 clinical trial and related regulatory discussions, we plan to initiate a Phase 2 clinical trial for OTX-TKI in Australia. We generally plan to conduct our later stage and pivotal clinical trials of our product candidates in the United States.

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.

Other risks inherent in conducting international clinical trials include:

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

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 extended-delivery drug delivery product candidates or any other product candidates that we may develop, 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 patients 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.

For example, we applied for a deferral from the FDA for the requirement to conduct pediatric studies for DEXTENZA for the treatment of post-surgical ocular inflammation and pain following cataract surgery until after approval of such product in adult populations for that indication. While the FDA ultimately approved our request, if the FDA had required us to conduct pediatric studies in advance of FDA approval in adult populations, we would have experienced significant delays in our ability to obtain marketing approval for DEXTENZA for these indications, particularly in light of our decision announced in November 2019 to postpone our clinical trial to evaluate DEXTENZA in pediatric subjects following cataract surgery until the fourth quarter of 2020. We will face a similar risk if we seek a comparable deferral for other product candidates or indications.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, 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 patients 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 local programmed-release drug delivery product candidates or our other product candidates that we may develop if we are unable to locate and enroll a sufficient number of eligible patients 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 patient enrollment. For example, in the third quarter of 2017, we initiated a Phase 1 clinical trial of OTX-TIC outside the United States. After several months, after not enrolling any patients, we closed this trial in the second quarter of 2018. Additionally, we intended to initiate our ongoing Phase 1 clinical trial of OTX-TKI outside the United States in 2018, but we were unable to start dosing patients until the first quarter of 2019.

A variety of factors affect patient enrollment, including:

- the prevalence and severity of the ophthalmic disease or condition under investigation;
- the 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 patients;
- 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 patients.

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 completed Phase 3 clinical trial of OTX-TP, the largest clinical trial we have conducted to date, was significantly slower than expected. It had a target enrollment of 550 patients and was conducted at approximately 49 sites in the United States.

Our inability to enroll a sufficient number of patients 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 would cause the value of our company to decline and limit our ability to obtain additional financing.

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

If DEXTENZA or any of our other 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. In each of our first two Phase 3 clinical trials of DEXTENZA for the treatment of post-surgical ocular inflammation and pain following cataract surgery, there were two subjects that experienced serious adverse events in the DEXTENZA group in each trial, none of which were ocular in nature or considered by the investigator to be related to the study treatment. In our third Phase 3 clinical trial of DEXTENZA for the treatment of post-surgical ocular inflammation and pain, there were three subjects that experienced serious adverse events in the DEXTENZA group, one of which was ocular in nature and none of which were considered by the investigator to be related to the study treatment. There was one ocular serious adverse event in the vehicle control group in the three completed Phase 3 clinical trials, which was hypopyon, or inflammatory cells in the anterior chamber. In our earlier Phase 2 clinical trial of DEXTENZA for the same indication, there were three serious adverse events, none of which was considered by the investigator to be related to the study treatment. In the DEXTENZA group of this Phase 2 clinical trial of DEXTENZA, the only adverse event that occurred more than once for the same subject was reduced visual acuity, which occurred twice but was not considered by the investigator to be related to the study treatment.

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 products and product candidates based on our bioresorbable hydrogel technology platform other than DEXTENZA and ReSure Sealant or expand the use of our bioresorbable hydrogel technology for treating additional diseases and conditions.

We are currently directing most of our development efforts towards applying our proprietary, bioresorbable hydrogel technology platform 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 products and product candidates at various stages of development based on our bioresorbable hydrogel technology platform and are exploring the potential use of our platform for other ophthalmic diseases and conditions. These 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 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 collaboration with Regeneron focuses on the development and potential commercialization of products to be delivered to the suprachoroidal space containing our extended-delivery hydrogel formulation in combination with Regeneron's large molecule VEGF-targeting compounds for the treatment of retinal diseases.

Our existing product candidates and any other potential product candidates that we or our collaborators identify 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. We are also considering the future growth potential of the hydrogel platform technology in new areas of the body. If we do not successfully develop and commercialize our products and product candidates that we or our current or future collaborators develop based upon our technological approach, we will not be able to obtain substantial product revenues or revenue from collaboration agreements, including our collaboration with Regeneron, in future periods.

We may expend our limited resources to pursue a particular product, 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. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities.

As part of our restructuring plan announced in November 2019, we decided to defer certain development programs as part of an initiative to reduce expenses and prioritize our resources to focus on commercializing DEXTENZA for post-surgical ocular inflammation and pain as well as completing the ongoing Phase 3 clinical trial of DEXTENZA for the treatment of ocular itching associated with allergic conjunctivitis, a Phase 1 clinical trial of OTX-TIC for the treatment of glaucoma and ocular hypertension, and a Phase 1 clinical trial of OTX-TKI for the treatment of wet AMD. Our prioritization of these programs, at the expense of others, during our restructuring may have delayed programs such as OTX-CSI and OTX-DED that we are now seeking to develop.

Similarly, we are now prioritizing the continued commercialization of DEXTENZA and the advancement through Phase 2 clinical development of each of OTX-TKI for the treatment of wet AMD, OTX-TIC for the treatment of glaucoma or ocular hypertension, 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. Although we believe such prioritization is currently the best use of our resources, we may not be correct.

Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product or product candidate, we may relinquish valuable rights to that product or 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 products or product candidate.

Risks Related to Manufacturing

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, ReSure Sealant and our product candidates for use in clinical trials, research and development and commercial efforts at our 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 its facilities inspection program 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 and requirements in connection with subsequent applications for other product candidates or DEXTENZA for additional indications or in connection with periodic, routine inspections for products for which we have received marketing authorization.

For example, as our facility is an approved pharmaceutical and medical device commercial manufacturing location, we are subject to routine inspections and system audits in connection with, among other things, our Safety, Identity, Strength, Purity, and Quality, or SISPQ; our process controls; and our standard operating procedures. If we fail to respond or comply in a satisfactory manner with any directives or observations that we may receive from the FDA as a result of inspections or informational requests, the FDA may take regulatory or other actions that would adversely impact our ability to continue manufacturing our commercial products and clinical or preclinical product candidates or to otherwise hinder or delay the clinical development and commercialization of our products and product candidates. In February 2021, the FDA requested information and records from us relating to our DEXTENZA commercial manufacturing operations and quality systems pursuant to Form 4003 in advance or in lieu of a drug inspection. In early March 2021, the FDA provided confirmation of receipt of the records that had been requested from us. Due to the COVID-19 pandemic, this Form 4003 process could be performed in lieu of an onsite inspection. However, the process is ongoing, will take time to complete, and is uncertain as to outcome. Regardless of the outcome of this informational request process, we could still be subject to an onsite inspection.

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, ReSure Sealant and our product candidates that we manufacture.

Any manufacturing defect, failure against SISPQ, 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.

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

If our 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 clinical or commercial supply. Such an event could delay our clinical trials or reduce our product sales.

Currently, we maintain insurance coverage against damage to our property and equipment in the amount of up to $27.5 million and to cover business interruption and research and development restoration expenses in the amount of up to $2.8 million. 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, ReSure Sealant, or any of our product candidates if there were a catastrophic event or failure of our current manufacturing facility or processes.

We expect to continue to contract with third parties for at least some aspects of the production 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, ReSure Sealant and our product candidates for commercialization and preclinical testing and clinical trials, including our supply of the active pharmaceutical ingredient drug substance PEG, the molecule that forms the basis of our hydrogels, and other raw materials and for sterilization of the finished product. In addition, while we believe that our existing manufacturing facility, or additional facilities that we will be able to build, will be sufficient to meet our requirements for manufacturing DEXTENZA, ReSure Sealant 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 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, ReSure Sealant 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. 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. In particular, 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 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.

Our potential future dependence upon others for the manufacture of our products and product candidates 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 Commercialization

Even though DEXTENZA and ReSure Sealant have received marketing approval from the FDA and even if any of our product candidates receives marketing approval, any of 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 and DEXTENZA for the treatment of post-surgical ocular inflammation and pain in July 2019 and cannot yet accurately predict whether either product will gain market acceptance and become commercially successful. For example, we previously commenced commercialization in Europe of an earlier version of ReSure Sealant that was approved and marketed as an ocular bandage. We recognized $0.1 million of revenue from the commercialization of this product through 2012. However, we ceased our commercialization of the product in 2012 to focus on the ongoing clinical development of ReSure Sealant pursuant to FDA requirements. If our products do not achieve an adequate level of acceptance, we may not generate significant product revenue and we may not become profitable.

The degree of market acceptance of DEXTENZA, ReSure Sealant, 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 and, for DEXTENZA and ReSure Sealant, the lack of separate reimbursement when used as part of a cataract surgery procedure;
- 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, it is possible that the market acceptance of DEXTENZA could be less than if we had conducted such a trial. We also have not conducted a clinical trial directly comparing the effectiveness of DEXTENZA to currently approved alternative treatments for ocular itching associated with allergic conjunctivitis. Although market research we have commissioned indicates that a majority of ophthalmologists believe DEXTENZA could become a new standard of care for post-surgical ocular inflammation and pain due to its potential ability to improve compliance with limited toxicity concerns, market acceptance for DEXTENZA could be substantially less than such research indicates, and we may not be able to achieve the market share we anticipate.

Our assessment of the potential market opportunity for DEXTENZA, ReSure Sealant 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, ReSure Sealant 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, ReSure Sealant, 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, ReSure Sealant, 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 focuses on ambulatory surgical centers responsible for the largest volumes of cataract surgery.

If we decide to commercialize any of our products outside of the United States, we would expect to utilize a variety of collaboration, distribution and other marketing arrangements with one or more third parties to commercialize any product that receives marketing approval. We expect that our existing sales force will be able to effectively market and sell DEXTENZA for the treatment of ocular itching associated with allergic conjunctivitis, if our sNDA is approved. We also intend to rely on Regeneron to commercialize our extended-delivery hydrogel formulation in combination with Regeneron's large molecule VEGF-targeting compounds.

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 OTX-TIC, 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, including our collaboration with Regeneron, 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 sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing DEXTENZA, ReSure Sealant 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. Given that we are developing products based on FDA-approved therapeutic agents, our products and product candidates, if approved, will face competition from generic and branded versions of existing drugs based on the same active pharmaceutical ingredients 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, other than those developed under the Regeneron collaboration, 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 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 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.

Icon Biosciences, Inc. received FDA approval of DEXYCU in February 2018. DEXYCU is an injection of dexamethasone into the anterior chamber of the eye to treat inflammation associated with cataract surgery. Other companies have also advanced into Phase 3 clinical development biodegradable, programmed-release drug delivery product candidates that could compete with our intracanalicular insert products and product candidates. ReSure Sealant is the first and only surgical sealant approved as a device for ophthalmic use in the United States, but will compete with sutures as an alternative method for closing ophthalmic wounds. Multiple companies, including our collaborator Regeneron, 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.

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 or are less expensive than our products. 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 and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

DEXTENZA, ReSure Sealant 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, ReSure Sealant 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, ReSure Sealant 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, ReSure Sealant 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, ReSure Sealant 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, ReSure Sealant 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. ReSure Sealant is not separately reimbursed when used as part of a cataract surgery procedure, which could limit the degree of market acceptance of this product by surgeons. DEXTENZA is currently

considered a post-surgical product, in the same fashion as eye drops. However, if DEXTENZA were instead categorized as an inter-operative product, it would not be subject to separate reimbursement in ambulatory surgical centers and hospital out-patient departments, which could likewise limit its market acceptance. DEXTENZA is currently scheduled to lose transitional pass-through status in July 2022. If pass-through status were to lapse, DEXTENZA would no longer be reimbursed separately from the ophthalmic surgery and our ability to generate revenues from the sales of DEXTENZA to ambulatory surgical centers and hospital out-patient departments for the treatment of post-surgical ocular inflammation and pain would be adversely affected.

A specific and permanent J-Code for ophthalmic inserts containing dexamethasone including DEXTENZA is in effect. Separately, a CPT procedure code has been established for the administration of drug-eluting intracanalicular inserts to facilitate reimbursement for physicians for the procedure of inserting DEXTENZA into the canaliculus. 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, 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 product candidates or products 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 patients;
- 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 $10.0 million in U.S. product liability insurance coverage in the aggregate, with a per incident limit of $10.0 million and approximately $15.0 million in product liability insurance in another jurisdiction in which we operate, with a per incident liability limit of approximately $15.0 million. These policies may not be adequate to cover all liabilities that we may incur. We will need to increase our insurance coverage as we expand our clinical trials and our sales of DEXTENZA, ReSure Sealant and any product candidates for which we obtain marketing approval.

We will need to further increase our insurance coverage if we commence commercialization of any of our product candidates for which we obtain marketing approval. Insurance coverage is increasingly expensive. 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 Our Dependence on Third Parties

We will depend heavily on our collaboration with Regeneron for the success of our extended-delivery hydrogel formulation in combination with Regeneron's large molecule VEGF-targeting compounds. If Regeneron does not

exercise its option, terminates our collaboration agreement or is unable to meet its contractual obligations, it could negatively impact our business.

In October 2016, we entered into a strategic collaboration, option and license agreement with Regeneron for the development and potential commercialization of products containing our extended-delivery hydrogel formulation in combination with Regeneron's large molecule VEGF-targeting compounds. We and Regeneron amended this agreement in May 2020 to, among other things, transition joint efforts under the collaboration to the research and development of an extended-delivery formulation of aflibercept to be delivered to the suprachoroidal space. We refer to the collaboration, option and license agreement, as amended to date, as the Regeneron Collaboration Agreement.

Our ability to generate revenues from the Regeneron Collaboration Agreement will depend on our and Regeneron's abilities to successfully perform the functions assigned to each of us under it. We did not receive any upfront payment under the Regeneron Collaboration Agreement. Regeneron has agreed to pay personnel and material costs for specified preclinical development activities under the collaboration, and Regeneron has an option to enter into an exclusive, worldwide license, with the right to sublicense, under our intellectual property to develop and commercialize products containing our extended-delivery hydrogel formulation in combination with Regeneron's large molecule VEGF-targeting compounds. Regeneron has agreed to pay us $10 million upon exercise of the option. As amended, the option is now exclusive until May 8, 2022, twenty-four months from the effective date of the amendment. We are also entitled to receive under the terms of the Regeneron Collaboration Agreement specified development, regulatory and sales milestone payments, as well as royalty payments.

If Regeneron exercises the option, the Regeneron Collaboration Agreement will expire on a licensed product-by-licensed product and country-by-country basis upon the expiration of the later of 10 years from the date of first commercial sale in such country or the expiration of all patent rights covering the licensed product in such country. Regeneron may terminate the Regeneron Collaboration Agreement at any time after exercise of the option upon 60 days' prior written notice. Either party may, subject to a cure period, terminate the Regeneron Collaboration Agreement in the event of the other party's uncured material breach, in addition to other specified termination rights.

If we are unable to achieve the preclinical milestones set forth in the collaboration plan, Regeneron may not exercise the option, in which case we would not receive the $10 million payment in connection with such option and would have incurred significant development expenses. Even if Regeneron does exercise its option, we or Regeneron may not be successful in achieving the necessary preclinical, clinical, regulatory and sales milestones in connection with the collaboration. Further, if Regeneron were to breach or terminate the Regeneron Collaboration Agreement or if Regeneron elects not to exercise the option we granted it and not to proceed in the collaboration, we may not be able to obtain, or may be delayed in obtaining, marketing approvals for intravitreal implant product candidates developed pursuant to the Regeneron Collaboration Agreement and will not be able to, or may be delayed in our efforts to, successfully commercialize our intravitreal implant product candidates. We may not be able to seek and obtain a viable, alternative collaborator to partner with for the development and commercialization of the licensed products on similar terms or at all.

We have entered into collaborations with third parties to develop certain product candidates, and in the future may enter into collaborations with third parties for the commercialization of DEXTENZA, ReSure Sealant or the development or commercialization of our product candidates. 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 collaborations with Regeneron and AffaMed, and expect to utilize a variety of types of collaboration, distribution and other marketing arrangements with third parties to commercialize DEXTENZA, ReSure Sealant, 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 our products and product candidates 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 other product candidates. 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. Other than our collaborations with Regeneron and AffaMed, we are not currently party to any such arrangement. 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 collaborations with Regeneron and AffaMed pose, 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 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, our development of our products or product candidates could be delayed

and we may need additional resources to develop our products or product candidates. All of the risks relating to product development, regulatory approval and commercialization described in this prospectus supplement also apply to the activities of our collaborators.

Additionally, subject to its contractual obligations to us, if a collaborator of ours were to be involved in a business combination, it might deemphasize or terminate the development or commercialization of any product or product candidate licensed to it by us. 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.

For some of our other product candidates, we may decide to collaborate with pharmaceutical, biotechnology and medical device companies for the development and potential commercialization of those 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 patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, 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 future license agreements from entering into agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. 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.

We have conducted preclinical testing of protein-based anti-VEGF compounds in collaboration with Regeneron to explore the feasibility of delivering their drugs in combination with our hydrogel. The initial drug selected for preclinical testing under this collaboration was aflibercept, marketed under the brand name Eylea. We may explore broader collaborations for the development and potential commercialization of our hydrogel technology in combination with other large molecules with targets other than VEGF for the treatment of back-of-the-eye diseases and conditions.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. 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, including our clinical trials for ReSure Sealant and our clinical trials for DEXTENZA for the treatment of post-surgical ocular inflammation and pain following cataract surgery. However, we have relied on third parties, such as CROs, to conduct clinical trials of certain of our product candidates, including DEXTENZA for the treatment of ocular itching associated with allergic conjunctivitis, and we may continue to do so. If we deem necessary, we may engage 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 would 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 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. For example, in May 2020, we disclosed the receipt of interim data regarding our ongoing Phase 1 clinical trial of OTX-TKI for the potential treatment of wet AMD and other retinal diseases. In July 2020, however, we received further, and partially contradictory, information from the clinical trial site where certain patients were being treated. As the clinical trial site had not entered certain data concerning these patients into the clinical trial database in a timely manner, complete information was not available to or known by us at the time of our prior disclosures. We are also required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. 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. Some of our licensed patents that we believe are integral to our hydrogel technology platform have terms that extend through at least 2024. However, other broader patents within our patent portfolio have already expired. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting our candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio would be less effective in excluding others from commercializing products similar or identical to ours. 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 will fail to identify patentable aspects of our research and development output 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 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, European Patent Office, 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. For example, unlike patent law in the United States, European patent law precludes the patentability of methods of treatment of the human body and imposes substantial restrictions on the scope of claims it will grant if broader than specifically disclosed embodiments. Moreover, we have no patent protection and likely will never obtain patent protection for ReSure Sealant outside the United States and Canada. We have only three issued patents outside of the United States that cover all three intracanalicular insert products and product candidates. We have three licensed patent families in Europe and certain other parts of the world for our intravitreal drug delivery product candidates, but only one patent issuance to date outside 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.

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 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. In particular, during prosecution of any patent application, the issuance of any patents based on the application may depend upon our ability to generate additional preclinical or clinical data that support the patentability of our proposed claims. We may not be able to generate sufficient additional data on a timely basis, or at all. 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.

Recent 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 recently 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 a new 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 initial 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 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. 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 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. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Because the active pharmaceutical ingredients in our products and product candidates other than those being developed pursuant to the Regeneron Collaboration Agreement 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 our patents or any patents that we license. These patents largely relate to the hydrogel composition of our intracanalicular inserts and the drug-release design scheme of our 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 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 patents or other intellectual property, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our licensed patents or other intellectual property. As a result, to counter infringement or unauthorized use, we may be required to 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. There is considerable intellectual property litigation in the biotechnology, medical device, and pharmaceutical industries. 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 DEXTENZA, ReSure Sealant or any of our 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 three 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 the claims of one of more 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 a claim 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. We have settled the legal proceedings related to one of these patents. The USPTO decided to proceed with the administrative proceeding related to one of the patents while declining to do so for the other. In June 2020, the PTAB, after an *inter partes* review, determined that we had proven by a preponderance of the evidence that all claims of such patent at issue held by such third party were invalid; the third party has appealed this decision. We continue to believe that DEXTENZA does not infringe the claims of the remaining patent 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 obtain a license from such third party to continue developing and marketing our products and technology. 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. 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 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 a significant portion of our patent rights and the technology for DEXTENZA, ReSure Sealant and our 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 develop, 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. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to

bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

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. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

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 inside and outside the United States 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.

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 agencies 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 have not received approval to market DEXTENZA for any other indications. We may determine to seek a CE Certificate of Conformity, which demonstrates compliance with relevant requirements and

provides approval to commercialize ReSure Sealant in the European Union. If we are unable to obtain a CE Certificate of Conformity for DEXTENZA, ReSure Sealant, or any of our 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, especially if additional clinical trials are required, 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. In addition, while we have had general discussions with the FDA concerning the design of some of our clinical trials, we have not discussed with the FDA the specifics of the regulatory pathways for our product candidates.

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. During the first of these inspections, the FDA identified storage temperature excursions for the investigational product that is labeled to be stored in a refrigerated condition between two degrees and eight degrees Celsius. We also had previously addressed a minor temperature deviation report during the conduct of the Phase 3 trials and communicated a response to the trial sites. In addition, while investigating the report stemming from the FDA inspection, several more noteworthy temperature excursions were found to have occurred that had not been fully reported. Because of the limited nature of the temperature excursions and historical product testing, including testing on product stored at elevated temperatures, we believe it is unlikely that drug product performance was significantly impacted. We have also implemented a corrective action plan to address clinical compliance and prevent recurrence in other clinical studies.

The FDA also completed two inspections of our manufacturing facility in connection with our NDA for DEXTENZA for the treatment of post-surgical ocular pain. After each inspection, we received a Form 483 from the FDA pertaining to deficiencies in our manufacturing processes identified during such inspection. After we responded to the issues which had been identified with corrective action plans, we subsequently received CRLs from the FDA. We may be subject to similar inspections in the future for DEXTENZA or for other product candidates for which we seek FDA approval. For example, in February 2021, the FDA requested information and records from us relating to our DEXTENZA commercial manufacturing operations and quality systems pursuant to Form 4003 in advance or in lieu of a drug inspection. If we are unable to address any identified issues successfully or if the FDA determines that the actions we take to remediate any identified issues to be inadequate, our ability to commercialize any products could be limited, which could adversely affect our ability to achieve or sustain profitability.

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.

Finally, disruptions at the FDA and other agencies may prolong the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

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.

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 DEXTENZA, ReSure Sealant or our 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.

Additionally, we could face heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the recent withdrawal of the United Kingdom from the European Union, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union, the United Kingdom withdrew from the European Union, effective December 31, 2020. On December 24, 2020, the United Kingdom and European Union entered into a Trade and Cooperation Agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction. Since the regulatory framework for pharmaceutical products in the United Kingdom covering the quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing any product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for any product candidates, which could significantly and materially harm our business.

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. We, and any current or future collaborators, must therefore comply with requirements concerning advertising and promotion for any of our products for which we or our collaborators obtain marketing approval. Promotional communications with respect to drug products, biologics, and medical devices are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, if any of our product candidates receives marketing approval, the accompanying label may limit the approved use of our product, which could limit sales of the product.

The FDA required two post-approval studies as a condition for approval of our premarket approval application for ReSure Sealant. The first post-approval study, identified as the Clinical PAS, was to enroll at least 598 patients to confirm that ReSure Sealant can be used safely by physicians in a standard cataract surgery practice and to confirm the incidence of the most prevalent adverse ocular events identified in our pivotal study of ReSure Sealant in eyes treated with ReSure Sealant. We submitted the final study report of the Clinical PAS to the FDA in June 2016, and the FDA has confirmed the Clinical PAS has been completed. The second post-approval study, identified as the Device Exposure Registry Study, is intended to link to the Medicare database to ascertain if patients are diagnosed or treated for

endophthalmitis within 30 days following cataract surgery and application of ReSure Sealant. The Device Exposure Registry Study is required to include at least 4,857 patients. In December 2015, CMS denied our application for a tracking or research code for ReSure Sealant commercial use. In July 2016, the FDA approved the Device Exposure Registry Study protocol. We are required to provide periodic reports to the FDA on the progress of this post-approval study until it is completed. We initiated enrollment in this study in December 2016 and submitted our first progress report to FDA in January 2017. Due to difficulties in establishing an acceptable way to link ReSure Sealant to the Medicare database and lack of investigator interest, we have been unable to enroll trial sites and patients, collect patient data and report study data to the FDA. On October 18, 2018, we received a warning letter from the FDA, dated October 17, 2018, relating to our compliance with data collection and information reporting obligations in this study. We appealed the warning letter from the FDA. In December 2018, the FDA rejected our appeal. A teleconference was held with the FDA in January 2019 resulting in tentative agreement on a proposed retrospective registry study of endophthalmitis rates to satisfy the Device Exposure Registry Study requirements. In December 2019, we submitted the protocol for the agreed-upon retrospective study and the prospective study outline, as required per the terms of the warning letter. We received feedback from the FDA in February 2020 and responded to the FDA in March 2020. In May 2020, the FDA approved the protocol. Subsequently, we received a close-out letter from the FDA dated September 2, 2020. We completed the retrospective study in accordance with our agreement with the FDA and submitted the final study report for the Device Exposure Registry Study to the FDA in January 2021. Following review of the results from these post-approval studies, any concerns with respect to endophthalmitis that we are unable to address due to the lack of completion of the study would negatively affect our ability to commercialize ReSure Sealant. Failure by us to conduct the Device Exposure Registry Study to the FDA's satisfaction may result in withdrawal of the FDA's approval of ReSure Sealant or other regulatory action.

In addition, 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.

Accordingly, 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.

Violations of the United States Federal Food, Drug, and Cosmetic Act, or the FDCA, relating to the promotion or manufacturing of drug products, biologics or medical devices may lead to investigations by the FDA, Department of Justice, or DOJ, and state attorneys general alleging violations of the FDCA, federal and state healthcare fraud and abuse laws, as well as state consumer protection laws. In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or 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.

Non-compliance with European Union requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the European Union's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

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 DEXTENZA, ReSure Sealant 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, currently set at $5,500 to $11,000 per false claim;

- 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 and teaching hospitals, with data collection beginning in August 2013; 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.

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 some 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.

Among the provisions of the Patient Protection and Affordable Care Act, or ACA, of potential importance to our business and our drug candidates are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

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 2029 unless additional Congressional action is taken. The Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2020, and extended the sequester by one year, through 2030. 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 new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

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 Tax Cuts and Jobs Act of 2017, or the TCJA, 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 December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the Court of Appeals for the Fifth Circuit affirmed the lower court's ruling that the individual mandate portion of the ACA is unconstitutional and it

remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. Thereafter, the U.S. Supreme Court agreed to hear this case. Oral argument in the case took place on November 10, 2020. On February 10, 2021, the Biden Administration withdrew the federal government's support for overturning the ACA. A ruling by the U.S. Supreme Court is expected sometime this year. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

In addition, the CMS has proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. On November 30, 2018, CMS announced a proposed rule that would amend the Medicare Advantage and Medicare Part D prescription drug benefit regulations to reduce out of pocket costs for plan enrollees and allow Medicare plans to negotiate lower rates for certain drugs. Among other things, the proposed rule changes would allow Medicare Advantage plans to use pre authorization, or PA, and step therapy, or ST, for six protected classes of drugs, with certain exceptions, permit plans to implement PA and ST in Medicare Part B drugs; and change the definition of "negotiated prices" while adding a definition of "price concession" in the regulations. It is unclear whether these proposed changes we be accepted, and if so, what effect such changes will have on our business. 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 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. This Executive Order also directs the U.S. Department of Health and Human Services to create a special enrollment period for the Health Insurance Marketplace in response to the COVID-19 pandemic.

The prices of prescription pharmaceuticals in the United States and foreign jurisdictions is 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. To date, 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 drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for products. To those ends, President Trump issued several Executive Orders intended to lower the costs of prescription drug products. Certain of these Executive Orders are reflected in recently promulgated regulations, including an interim final rule implementing President Trump's most favored nation model, but such final rule is currently subject to a nationwide preliminary injunction. It remains to be seen whether these Executive Orders and resulting regulations will remain in force during the Biden Administration. Further, on September 24, 2020, the Trump Administration finalized a rulemaking allowing states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

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 health care 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 health care 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, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate 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 harmed, possibly materially.

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 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 all 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 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. 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 the European Union. The GDPR and other 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.

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.

As we expand our operations outside of the United States, such as we have begun to do with our collaboration with AffaMed, 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.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. Further, 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 the European Union. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of European Union Member States, such as the U.K. Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians 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. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

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.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with manufacturing standards we have established, to comply with federal and state health-care fraud and abuse laws and regulations, to report financial information or data accurately or to disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws 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.

If we, our collaborators or any third-party manufacturers we engage in the future fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur significant costs.

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

Although we maintain general liability insurance as well as workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Further, with respect to the operations of any current or future collaborators or third-party contract manufacturers, it is possible that if they fail to operate in compliance with applicable environmental, health and safety laws and regulations or properly dispose of wastes associated with our products, we could be held liable for any resulting damages, suffer reputational harm or experience a disruption in the manufacture and supply of our product candidates or products.

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, 2020, we had net operating loss, or NOL, carryforwards for federal and state income tax purposes of $354.7 million and $274.9 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 $229.1 million, can be carried forward indefinitely. As of December 31, 2020, we also had available research and development tax credit carryforwards for federal and state income tax purposes of $9.2

million and $5.0 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. As described below under the heading "*Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition*," the Tax Cuts and Jobs Act of 2017, or the 2017 Tax Act, as amended by the CARES Act, includes changes to U.S. federal tax rates and the rules governing NOL carryforwards that may significantly impact our ability to utilize our net operating losses, or NOLs, to offset taxable income in the future. Nor is it clear how various states will respond to the 2017 Tax Act; the Families First Coronavirus Response Act, or FFCR Act; or the CARES Act. In addition, state NOLs generated in one state cannot be used to offset income generated in another state. Furthermore, the use of NOL carryforwards may become subject to an annual limitation under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, and similar state provisions in the event of certain cumulative changes in the ownership interest of significant shareholders in excess of 50 percent over a three-year period. This could limit the amount of NOL carryforwards that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of a company immediately prior to the ownership change. We have not conducted a full 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. As a result, we are uncertain as to whether we have completed one or more transactions since our inception which may have resulted in an ownership change under Section 382 of the Code. In addition, there may be changes in our stock ownership, some of which are outside of our control, that could result in ownership changes in the future. For these reasons, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes.

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 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. We do not maintain "key person" insurance for any of our executives or other employees.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be 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 employers other than us 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.

We have in the past reduced the size of our organization, and we may be required to do so again in the future, which may cause us to encounter difficulties in managing our business as a result of any such reduction, or attrition that may occur following such reduction, which could disrupt our operations. In addition, we may not achieve anticipated benefits and savings from such a reduction.

In November 2019, we reduced our workforce by 55 employees, representing approximately 22% of our workforce. We completed the restructuring and recorded the restructuring charges in the fourth quarter of 2019. We may in the future be required to reduce the size of our organization as part of an initiative to reduce expenses and reprioritize our use of resources.

Any restructuring and additional measures we might take to reduce costs could divert management attention, yield attrition beyond our intended reduction if force, reduce employee morale, or cause us to delay, limit, reduce or eliminate certain product development plans.

We expect to expand our development, regulatory and manufacturing capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect our drug development, clinical, regulatory affairs, manufacturing and our sales and marketing capabilities to grow as we commercialize DEXTENZA and any product candidates that may receive marketing approval. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. We relocated our corporate headquarters to 24 Crosby Drive, Bedford, Massachusetts to accommodate our growth. We are evaluating expanding our manufacturing operations into 15 Crosby Drive, Bedford, Massachusetts while maintaining our existing operations located at 36 Crosby Drive, Bedford, Massachusetts. Due to our limited financial resources and our limited experience in managing such anticipated growth, we may not be able to effectively manage the expansion of our operations, or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Risks Related to Our Common Stock

Our executive officers, directors and principal stockholders, if they choose to act together, have the ability to control all matters submitted to stockholders for approval.

Our executive officers, directors and principal stockholders, in the aggregate, beneficially own a large portion of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets.

This concentration of voting power may:

- delay, defer or prevent a change in control;
- entrench our management and the board of directors; or
- delay or prevent a merger, consolidation, takeover or other business combination involving us on terms that other stockholders may desire.

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 recently 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.

The market prices of securities of companies in the biotechnology and pharmaceutical industry have been extremely volatile and have experienced fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. These fluctuations could adversely affect the market price of our common stock. 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 current and former executive officers and shareholder derivative actions were filed against certain of our current and former executive officers, certain of our current and former board members, 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. Around this time, we also received subpoenas from the Securities and Exchange Commission seeking documents and information concerning DEXTENZA, including related communications with the FDA and investors; in May 2019, the SEC notified us that it had concluded its investigation.

Due to the volatility in our stock price, we may be the target of similar proceedings in the future. In connection with 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 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, ReSure Sealant 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;
- results of clinical trials of 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 level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts and the efforts of our current and future collaborators to discover, develop, acquire or in-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;
- 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;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, political and social, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

In the past, following periods of volatility in the market price of a company’s securities, securities class-action litigation has often been instituted against that company. We also may face securities class-action litigation if we cannot obtain regulatory approvals for or if we otherwise fail to commercialize DEXTENZA or our other product candidates. These proceedings and other similar litigation, if instituted against us, could cause us to incur substantial costs to defend such claims and divert management’s attention and resources.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

Persons who were our stockholders prior to our initial public offering continue to hold a substantial number of shares of our common stock. If such persons sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline.

In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our stock incentive plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act of 1933, as amended, and, in

any event, we have filed a registration statement permitting shares of common stock issued on exercise of options to be freely sold in the public market. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

Certain holders of our common stock have rights, subject to specified conditions, to require us to file registration statements covering their shares or, along with certain holders of shares of our common stock issuable upon exercise of warrants issued to lenders, to include their shares in registration statements that we may file for ourselves or other stockholders. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

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

We are a "smaller reporting company," as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended. We would cease to be a smaller reporting company if we have a non-affiliate public float in excess of $250 million and annual revenues in excess of $100 million, or a non-affiliate public float in excess of $700 million, determined on an annual basis. As a smaller reporting company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not smaller reporting companies. These exemptions include:

- being permitted to provide only two years of audited consolidated financial statements in this Annual Report on Form 10-K, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- reduced disclosure obligations regarding executive compensation;
- not being required to furnish a contractual obligations table in "Management's Discussion and Analysis of Financial Condition and Results of Operations"; and
- not being required to furnish a stock performance graph in our annual report.

We expect to continue to take advantage of some or all of the available exemptions until we cease to be a smaller reporting company.

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

We incur increased costs as a result of operating as a public company, and our management is now required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, we incur and will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and will make some activities more time-consuming and costly.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting. On January 1, 2020, we became subject to the requirement to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm because we were no longer an emerging growth company. Although the SEC has provided smaller reporting companies relief from this requirement to include an attestation report in March 2020, to maintain compliance with other provisions of Section 404, we will continue to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the

adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor, if required, our independent registered public accounting firm will be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we or our independent registered public accounting firm identify one or more material weaknesses in our internal control over financial reporting, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our consolidated financial statements.

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.

General Risk Factors

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

Our internal computer systems and those of our current and any future collaborators, contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our products and product candidates could be delayed.

Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition.

Changes in tax law may adversely affect our business or financial condition. On December 22, 2017, President Trump signed the 2017 Tax Act into law, which significantly revised the Internal Revenue Code of 1986, as amended. The 2017 Tax Act, among other things, contained significant changes to corporate federal income taxation, including the reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, the limitation of the tax deduction for net interest expense to 30% of adjusted earnings (except for certain small businesses), the limitation of the deduction for NOLs to 80% of current year taxable income and elimination of NOL carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such NOLs may be carried forward indefinitely), the imposition of one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, the elimination of U.S. tax on foreign earnings (subject to certain important exceptions), the allowance of immediate deductions for certain new investments instead of deductions for depreciation expense over time, and the modification or repeal many business deductions and credits.

As part of Congress' response to the COVID-19 pandemic, the Families First Coronavirus Response Act, or FFCR Act, was enacted on March 18, 2020, and the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, was enacted on March 27, 2020. Both contain numerous tax provisions. In particular, the CARES Act retroactively and temporarily (for taxable years beginning before January 1, 2021) suspends application of the 80%-of-income limitation on the use of NOLs, which was enacted as part of the 2017 Tax Act. It also provides that NOLs arising in any taxable year beginning after December 31, 2017, and before January 1, 2021 are generally eligible to be carried back up to five years. The CARES Act also temporarily (for taxable years beginning in 2019 or 2020) relaxes the limitation of the tax deductibility for net interest expense by increasing the limitation from 30 to 50% of adjusted taxable income.

Regulatory guidance under the 2017 Tax Act, the FFCR Act and the CARES Act is and continues to be forthcoming, and such guidance could ultimately increase or lessen impact of these laws on our business and financial condition. It is also likely that Congress will enact additional legislation in connection with the COVID-19 pandemic, some of which could have an impact on our company. In addition, it is uncertain if and to what extent various states will conform to the 2017 Tax Act, the FFCR Act or the CARES Act.

Item 1B. Unresolved Staff Comments

None.

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 space expires in July 2027, the lease for approximately 30,000 square feet of space expires in 2024, and the lease for approximately 20,000 square feet of space expires in 2023. We believe that our 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

None.

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 1, 2021, there were approximately 20 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.

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, 2020 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.

In February 2021, we issued an employee non-statutory stock options to purchase up to 150,000 shares of our common stock outside our 2014 Stock Incentive Plan and under our 2019 Inducement Stock Incentive Plan as an inducement material to the individual's acceptance of an offer of employment with us in accordance with Nasdaq Listing Rule 5635(c)(4). We intend to file a registration statement on a Form S-8 to register the shares of common stock underlying this inducement award prior to the time at which the award becomes exercisable.

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. Selected Financial Data

Not applicable.

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

We are a biopharmaceutical company focused on the formulation, development and commercialization of innovative therapies for diseases and conditions of the eye using our proprietary, bioresorbable hydrogel platform technology. We use this technology to tailor duration and amount of delivery of a range of therapeutic agents in our product candidates.

We currently incorporate therapeutic agents that have previously received regulatory approval from the U.S. Food and Drug Administration, or FDA, including small molecules and proteins, into our hydrogel technology with the goal of providing local programmed-release of drug to the eye. We believe that our local programmed-release drug delivery technology has the potential to treat conditions and diseases of both the front and the back of the eye and can be administered through a range of different modalities including intravitreal implants, suprachoroidal implants, intracameral implants and intracanalicular inserts. We have product candidates in preclinical and clinical development designed to utilize this technology to treat retinal diseases including wet age-related macular degeneration, or wet AMD; glaucoma and ocular hypertension; and ocular surface diseases and conditions including chronic and acute dry eye disease and ocular itching associated with allergic conjunctivitis. We also have two FDA-approved products in commercialization in the United States: DEXTENZA®, an intracanalicular insert for the treatment of post-surgical ocular inflammation and pain, and ReSure® Sealant, an ophthalmic device designed to prevent wound leaks in corneal incisions following cataract surgery. Our core pipeline assets include four development programs. We are currently evaluating two of these programs in Phase 1 clinical trials: OTX-TKI, an intravitreal implant injected by fine-gauge needle of a hydrogel, anti-angiogenic formulation of axitinib, a tyrosine kinase inhibitor, or TKI, for the treatment of wet AMD, and OTX-TIC, a travoprost intracameral implant for the reduction of intraocular pressure, or IOP, in patients with primary open-angle glaucoma or ocular hypertension. We have commenced Phase 2 clinical trials of OTX-CSI, a cyclosporine intracanalicular insert for the chronic treatment of dry eye disease, and OTX-DED, a dexamethasone intracanalicular insert for the short-term treatment of the signs and symptoms of dry eye disease.

We also have a collaboration with Regeneron Pharmaceuticals, Inc., or Regeneron, for the development and potential commercialization of products containing our extended-delivery hydrogel in combination with Regeneron's large molecule vascular endothelial growth factor, or VEGF, inhibitor, aflibercept, currently marketed under the brand name Eylea. On May 8, 2020, we entered into an amendment to our existing collaboration agreement with Regeneron. Pursuant to this amendment, we and Regeneron have adopted a new workplan to transition joint efforts under the existing collaboration agreement to the research and development of an extended-delivery formulation of aflibercept to be delivered to the suprachoroidal space. Regeneron has agreed to pay for our personnel and material costs for specified preclinical development activities in connection with the revised workplan, as well as costs of certain specialty equipment.

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 filed a supplemental New Drug Application, or sNDA, in the fourth quarter of 2020 for an additional indication of DEXTENZA for the treatment of ocular itching associated with allergic conjunctivitis. The FDA has accepted our sNDA for filing and has established a target action date under the Prescription Drug User Fee Act, commonly known as PDUFA, of October 18, 2021.

In October 2020, we entered into a license agreement and collaboration with AffaMed Therapeutics Limited, or AffaMed, for the development and commercialization of DEXTENZA and OTX-TIC in mainland China, Hong Kong, Macau, and Taiwan; South Korea, and the ASEAN markets (Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, the Philippines, Singapore, Thailand and Vietnam).

We continue to assess the potential use of our hydrogel platform technology in other areas of the body.

Business Update Regarding COVID-19

The pandemic caused by an outbreak of a new strain of coronavirus, or the COVID-19 pandemic, that is affecting the U.S. and global economy and financial markets and the related responses of government, businesses and individuals are also impacting our employees, patients, communities and business operations. The implementation of travel bans and restrictions, quarantines, shelter-in-place/stay-at-home and social distancing orders and shutdowns, for example, affected our business in 2020. The full extent to which the COVID-19 pandemic will continue to directly or indirectly impact our business, results of operations and financial condition and those of our customers, vendors, suppliers, and collaboration partners in 2021 will depend on future developments that are highly uncertain and cannot be accurately predicted, including new information that may emerge concerning COVID-19, the actions taken to contain it or treat its impact and the economic impact on local, regional, national and international markets. Management continues to actively monitor this situation and the possible effects on our financial condition, liquidity, operations, suppliers, industry, and workforce. In the paragraphs that follow, we have described impacts of the COVID-19 pandemic on our clinical development programs. For additional information on risks posed by the COVID-19 pandemic, please see "Item 1A — Risk Factors — Risks Related to the Coronavirus Pandemic," included elsewhere in this Annual Report on Form 10-K.

Financial Position

We have local programmed-release drug delivery product candidates in preclinical and clinical development, and we have two FDA-approved products—DEXTENZA, an intracanalicular insert for the treatment of post-surgical ocular inflammation and pain, and ReSure Sealant, an ophthalmic device designed to prevent wound leaks in corneal incisions following cataract surgery—in commercialization in the United States. Our ability to generate product revenues sufficient to achieve profitability will depend heavily on our continued commercialization of DEXTENZA for the treatment of ocular inflammation and pain following ophthalmic surgery and our obtaining marketing approval for and commercializing other products with significant market potential, including DEXTENZA for the treatment of ocular itching associated with allergic conjunctivitis, OTX-TKI for the treatment of wet AMD, OTX-TIC for the treatment of glaucoma and ocular hypertension, 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. Since inception, we have incurred significant operating losses. Our net losses were $155.6 million and $86.4 million for the years ended December 31, 2020 and 2019, respectively. As of December 31, 2020, we had an accumulated deficit of $539.3 million.

Our total cost and operating expenses were $80.3 million and $90.0 million for the years ended December 31, 2020 and 2019, respectively, including $7.5 million and $8.8 million, respectively, in non-cash stock-based compensation expense. Our operating expenses have grown as we continue to support the commercial launch of DEXTENZA following its entry into the market in July 2019; continue to pursue the clinical development of OTX-TKI, OTX-TIC, OTX-CSI, OTX-DED, OTX-AFS and DEXTENZA for the treatment of ocular itching associated with allergic conjunctivitis; continue the research and development of our other product candidates; and seek marketing approval for any such product candidate for which we obtain favorable pivotal clinical trial results. We expect to incur substantial sales and marketing expenses in connection with the ongoing DEXTENZA commercial launch and that of any of our other product candidates. In addition, we will continue to incur additional costs associated with operating as a public company, including legal costs associated with any pending legal proceedings.

Although we expect to generate revenue from sales of DEXTENZA and limited revenue from sales of ReSure Sealant, we will need to obtain substantial additional funding to support our continuing operations and the commercialization of DEXTENZA. If we are unable to raise capital or access our borrowing capacity when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts or to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us.

Through December 31, 2018, we raised $337.7 million through the sale of common stock in various offerings and $25.0 million through a credit facility.

In November 2016, we entered into a controlled equity offering sales agreement, or the 2016 Sales Agreement, with Cantor Fitzgerald & Co., or Cantor, under which we could offer and sell our common stock having aggregate proceeds of up to $40.0 million from time to time. During 2019, we sold 1,318,481 shares of common stock pursuant to the 2016 Sales Agreement, resulting in net proceeds of approximately $5.0 million after underwriting discounts and commissions and expenses. As of February 25, 2019, we had no amounts remaining available for future sale under the 2016 Sales Agreement. On February 28, 2019, pursuant to the 2016 Sales Agreement, we delivered a termination notice to Cantor, terminating the 2016 Sales Agreement. Through March 31, 2019, we sold an aggregate of 6,330,222 shares of common stock under the 2016 Sales Agreement, resulting in net proceeds of approximately $38.4 million after underwriting discounts and commissions and other offering expenses.

On March 1, 2019, we issued $37.5 million of unsecured senior subordinated convertible notes, or the 2026 Convertible Notes. The 2026 Convertible Notes accrue interest at an annual rate of 6% of their outstanding principal amount, payable at maturity, on March 1, 2026, unless earlier converted, repurchased or redeemed. The holders of the 2026 Convertible Notes may convert all or part of the outstanding principal amount of their 2026 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 2026 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, none of which have occurred to date.

On April 5, 2019, we entered into an Open Market Sale Agreement[SM], or the 2019 Sales Agreement, with Jefferies LLC, or Jefferies, under which we may offer and sell shares of our common stock having an aggregate offering price of up to $50.0 million from time to time through Jefferies, acting as agent. In the twelve months ended December 31, 2019, the Company sold 7,337,459 shares of common stock under the 2019 Sales Agreement, resulting in net proceeds of approximately $32.7 million, respectively, after commissions and expenses. In the twelve months ended December 31, 2020, the Company sold 2,984,381 shares of common stock under the 2019 Sales Agreement, resulting in net proceeds of approximately $14.4 million, respectively, after commissions and expenses. From inception to December 31, 2020, we have sold 10,321,840 shares of common stock under the 2019 Sales Agreement, resulting in net proceeds of approximately $47.0 million after commissions and expenses.

In May 2020, we entered into an underwriting agreement with Jefferies and Piper Sandler & Co., or the Underwriters, pursuant to which we issued and sold an aggregate of 9,409,091 shares of our common stock in an underwritten public offering at a public offering price of $5.50 per share. We refer to this offering as the May 2020 Offering. After deducting underwriting discounts and commissions and offering expenses, we received net proceeds from the May 2020 Offering of approximately $48.3 million.

In October 2020, we entered into an underwriting agreement with the Underwriters pursuant to which we issued and sold an aggregate of 8,257,000 shares of our common stock in an underwritten public offering at a public offering price of $9.75 per share. We refer to this offering as the October 2020 Offering. After deducting underwriting discounts and commissions and offering expenses, we received net proceeds from the October 2020 Offering of approximately $75.4 million.

In December 2020, we entered into an underwriting agreement with the Underwriters pursuant to which we issued and sold an aggregate of 4,283,750 shares of our common stock in an underwritten public offering at a public offering price of $21.50 per share. We refer to this offering as the December 2020 Offering. After deducting underwriting discounts and commissions and offering expenses, we received net proceeds from the December 2020 Offering of approximately $86.4 million.

We believe that our existing cash and cash equivalents of $228.1 million as of December 31, 2020, will enable us to fund our planned operating expenses, debt service obligations and capital expenditure requirements through 2023. This estimate is based on our current operating plan which includes estimates of anticipated cash inflows from DEXTENZA and ReSure Sealant product sales and cash outflows from operating expenses. These estimates are subject to various assumptions including those related to the severity and duration of the COVID-19 pandemic, the revenues and expenses associated with the commercialization of DEXTENZA, the pace of our research and clinical development programs, and other aspects of our business. These and other assumptions upon which we have based our estimate may prove to be wrong, and we could use our capital resources sooner than we currently expect and would therefore need to

raise additional capital to support our ongoing operations or adjust our plans accordingly. See "—Liquidity and Capital Resources."

Financial Operations Overview

Revenue

From our inception through December 31, 2020, we have generated limited amounts of revenue from the sales of our products. We commenced sales of ReSure Sealant in the first quarter of 2014, but we have received only limited revenues from ReSure Sealant to date and anticipate only limited sales for 2021. Until June 2019, ReSure Sealant was our only source of revenue from product sales.

We began to recognize limited product revenue from DEXTENZA during the second quarter of 2019 with the first commercial shipments to customers in June 2019. As further explained under "—Revenue Recognition—Product Revenue, Net" below, we recognize revenue when we sell DEXTENZA in the United States to a network of specialty distributors, who then resell the product to ambulatory surgical centers, or ASCs, and hospital outpatient departments, or HOPDs. We refer to these resales from the specialty distributors to the ASCs and HOPDs as in-market unit sales. For the first two months of 2021, in-market units sales neared 9,500, representing an increase of greater than 10% over the first two months of the fourth quarter of 2020. We may generate revenue in the future if we continue to commercialize DEXTENZA and develop and commercialize one or more of our product candidates and receive marketing approval for any such product candidate or if we enter into longer-term collaboration agreements with third parties.

For the year ended December 31, 2020, three specialty distributor customers accounted for 42%, 29% and 12% of our total revenue and three specialty distributor customers accounted for 45%, 33% and 15% of our total accounts receivable. No other customer accounted for more than 10% of total revenue or accounts receivable for the year ended December 31, 2020.

For the year ended December 31, 2019, two specialty distributor customers accounted for 27% and 11% of our total revenue and three specialty distributor customers accounted for 39%, 18% and 11% of our total accounts receivable. No other customer accounted for more than 10% of total revenue or accounts receivable for the year ended December 31, 2019.

Operating Expenses

Cost of Product Revenue

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

- Direct materials costs;
- Royalties;
- Direct labor, which includes employee-related expenses, including salaries, related benefits and payroll taxes, travel 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 platform technology, 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 patient 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.

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.

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, regulatory, compliance, director and officer insurance costs as well as investor and public relations expenses associated with being a public company.

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 and advertising and promotion costs. During the years ended December 31, 2020 and 2019, we incurred limited marketing expenses in connection with ReSure Sealant, which we began commercializing in 2014. Selling and marketing expenses for DEXTENZA increased in 2019 due to the product's July 2019 commercial launch and further increased in 2020 with the continued commercialization of DEXTENZA. We anticipate that our selling and marketing expenses associated with DEXTENZA will continue to increase, particularly as we plan to grow our salesforce supporting DEXTENZA in 2021.

Other Income (Expense)

Interest Income. Interest income consists primarily of interest income earned on cash and cash equivalents. In each of 2020 and 2019, our interest income has not been significant due to the low rates of interest being earned on our invested balances.

Interest Expense. Interest expense consists of interest expense on our debt. We borrowed $15.0 million in aggregate principal amount in April 2014. We refer to the credit facility under which we drew down this indebtedness, as amended over time, as our Credit Facility. In December 2015, we amended our credit and security agreement, which we refer to, as amended, as our Credit Agreement, to increase the aggregate principal amount borrowed under our Credit Facility to $15.6 million, extend the interest-only payment period through December 2016, and extend the maturity date to December 1, 2019. In March 2017, we amended our Credit Agreement to increase the aggregate principal amount borrowed under our Credit Facility to $18.0 million, extend the interest-only payment period through February 2018, and extend the maturity date to December 1, 2020. In December 2018, we amended the Credit Agreement to increase the aggregate principal amount borrowed under our Credit Facility to $25.0 million, extend the interest-only payment period through December 2020, and extend the maturity date to December 2023.

On March 1, 2019, we issued $37.5 million of the 2026 Convertible Notes. The 2026 Convertible Notes accrue interest at an annual rate of 6% of their outstanding principal amount, payable in cash at maturity, on March 1, 2026, unless earlier converted, repurchased or redeemed.

Change in Fair Value of Derivative Liability. In 2019, in connection with the issuance of our 2026 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 are recorded through the statement of operations and comprehensive loss and are presented under the caption change in fair value of

derivative liability. Our derivative liability calculations are further described under the heading "—Critical Accounting Policies and Significant Judgments and Estimates—Derivative Liability" below.

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 DEXTENZA for the treatment of post-surgical ocular inflammation and pain, which we began selling to customers in June 2019, and ReSure Sealant. We have generated limited revenues from ReSure Sealant to date and do not expect significant future sales.

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. In addition to distribution agreements with customers, we enter into arrangements with government payers that provide for government mandated 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 offers 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 its visibility into the inventory remaining in the distribution channel. We have received no 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.

Rebates— We offer rebate payments for which ASCs, HOPDs and other prescribers qualify by meeting purchase volumes of DEXTENZA under our rebate program. We calculate rebate payment amounts due under this program based on actual qualifying purchase and apply a contractual discount rate. The calculation of the accrual for rebates is based on an estimate of claims 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 an accrued expenses and other current liabilities on the consolidated balance sheets.

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 payers. 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 an accrued expenses and other current liabilities on the consolidated balance sheets.

Derivative Liability

The 2026 Convertible Notes allow the holders to convert all or part of the outstanding principal of their 2026 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 2026 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. 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.

Results of Operations

Comparison of the Years Ended December 31, 2020 and December 31, 2019

The following table summarizes our results of operations for the years ended December 31, 2020 and 2019:

	Year Ended December 31,		Increase (Decrease)
	2020	2019	
	(in thousands)		
Revenue:			
Product revenue, net	$ 17,403	$ 4,227	$ 13,176
Total revenue, net	17,403	4,227	13,176
Costs and operating expenses:			
Cost of product revenue	2,083	2,325	(242)
Research and development	28,694	41,091	(12,397)
Selling and marketing	26,614	24,491	2,123
General and administrative	22,859	22,122	737
Total costs and operating expenses	80,250	90,029	(9,779)
Loss from operations	(62,847)	(85,802)	22,955
Other income (expense):			
Interest income	168	1,229	(1,061)
Interest expense	(6,768)	(6,101)	(667)
Change in fair value of derivative liability	(86,189)	4,310	(90,499)
Other income (expense), net	—	(8)	8
Total other income (expense), net	(92,789)	(570)	(92,219)
Net loss	$ (155,636)	$ (86,372)	$ (69,264)

Gross-to-Net Deductions

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. Our total gross-to-net provisions for the years ended December 31, 2020 and 2019 were 22.2% and 16.3%, respectively, of gross DEXTENZA product sales. In 2020, we introduced a rebate program under a purchase volume-discount program that primarily relates to the change over the prior year in the gross-to-net provisions.

Chargebacks and Rebates

We record a provision for estimated chargebacks and rebates at the time we recognize DEXTENZA product sales revenue and reduce the accrual when payments are made or credits are granted. Our chargebacks are related to a pharmaceutical pricing agreement, a federal supply schedule agreement, a 340B prime vendor agreement, a Medicaid drug rebate agreement and beginning in 2020, rebates under our purchase volume-discount programs.

Distribution Fees and Product Return Allowances

We pay our wholesalers a distribution fee for services they perform for us based on the dollar value of their purchases of DEXTENZA. We record a provision for these charges as a reduction to revenue at the time of sale to the wholesaler and we issue a credit memo to the wholesaler against its outstanding receivable to us.

We record a provision for returns upon sale of DEXTENZA to our wholesaler. When a return or claim is received, we issue a credit memo to the wholesaler and reduce the corresponding liability.

Net Revenue

We generated $17.4 million of revenue during the year ended December 31, 2020 from sales of our products, of which $15.7 million was attributable to sales of DEXTENZA and $1.7 million was attributable to sales of ReSure

Sealant. We generated $4.2 million of product revenue during the year ended December 31, 2019, of which $2.2 million was attributable to DEXTENZA and $2.0 million was attributable to sales of ReSure Sealant during the year ended December 31, 2019. We began to recognize product revenue from DEXTENZA during the second quarter of 2019 with the first commercial shipments to customers in June 2019. The growth in revenue for DEXTENZA was due to increased market acceptance and commercialization efforts during 2020.

Research and Development Expenses

	Year Ended December 31,		Increase (Decrease)
	2020	2019	
	(in thousands)		
Direct research and development expenses by program:			
OTX-TKI for wet AMD	$ 1,534	$ 1,013	$ 521
OTX-TIC for glaucoma or ocular hypertension	924	726	198
OTX-CSI for treatment of dry eye disease	1,389	—	1,389
OTX-DED for the short-term treatment of the signs and symptoms of dry eye disease	111	—	111
DEXTENZA for post-surgical ocular inflammation and pain	1,077	1,039	38
DEXTENZA for ocular itching associated with allergic conjunctivitis	2,296	2,060	236
ReSure Sealant	117	153	(36)
OTX-TP for glaucoma and ocular hypertension	584	1,558	(974)
Preclinical activities	403	1,645	(1,242)
Unallocated expenses:			
Personnel costs	11,458	20,068	(8,610)
All other costs	8,801	12,829	(4,028)
Total research and development expenses	$ 28,694	$ 41,091	$ (12,397)

Research and development expenses were $28.7 million for the year ended December 31, 2020, compared to $41.1 million for the year ended December 31, 2019. The decrease of $12.4 million was primarily due to a decrease of $12.6 million in unallocated expenses. Unallocated research and development costs decreased $12.6 million for the year ended December 31, 2020, compared to the year ended December 31, 2019 primarily due to a decrease in unallocated personnel costs of $8.6 million and $4.0 million in all other costs as a result of the organizational restructuring that took place in November 2019 which reduced personnel and deferred program costs. For the year ended December 31, 2020, we incurred $8.0 million in direct research and development expenses for our product candidates compared to $6.5 million for the year ended December 31, 2019. The increase of $1.5 million is related to timing and start of our various clinical trials for our product candidates. We expect that clinical trial expenses will increase for our product candidates including for OTX-TKI due to the planned initiation of Phase 1 and Phase 2 clinical trials in mid-2021, for OTX-TIC due to the planned initiation of a Phase 2 clinical trial in mid-2021, for OTX-CSI due to the continuation of our Phase 2 clinical trial initiated in 2020, and for OTX-DED due to the initiation of our Phase 2 clinical trial in February 2021.

Selling and Marketing Expenses

	Year Ended December 31,		Increase (Decrease)
	2020	2019	
	(in thousands)		
Personnel related (including stock-based compensation)	$ 17331	$ 12,382	$ 4,949
Professional fees	5,996	9,087	(3,091)
Facility related and other	3,287	3,022	265
Total selling and marketing expenses	$ 26,614	$ 24,491	$ 2,123

Selling and marketing expenses were $26.6 million for the year ended December 31, 2020, compared to $24.5 million for the year ended December 31, 2019. The increase of $2.1 million was primarily due to an increase of $4.9 million in personnel costs, including stock-based compensation as the Company increased the field-based team to

support the commercial launch of DEXTENZA, partially offset by a decrease of $3.1 million in professional fees including consulting, trade shows, and conferences.

We expect our selling and marketing expenses to increase in 2021 and beyond, as we continue to support the commercial launch of DEXTENZA and, if our sNDA is approved, support the planned commercial launch of DEXTENZA for ocular itching associated with allergic conjunctivitis in the first half of 2022.

General and Administrative Expenses

	Year Ended December 31,		Increase (Decrease)
	2020	2019	
	(in thousands)		
Personnel related (including stock-based compensation)	$ 11,688	$ 11,352	$ 336
Professional fees	8,886	8,257	629
Facility related and other	2,285	2,513	(228)
Total general and administrative expenses	$ 22,859	$ 22,122	$ 737

General and administrative expenses were $22.9 million for the year ended December 31, 2020, compared to $22.1 million for the year ended December 31, 2019. The increase of $0.7 million was primarily due to an increase of $0.6 million in professional fees.

Other Income (Expense), Net

Other expense, net was $92.8 million for the year ended December 31, 2020, compared to $0.6 million for the year ended December 31, 2019. The change of $92.2 million, was due to an unrealized loss of $86.2 million on the change in fair value of the derivative liability associated with the 2026 Convertible Notes and lower interest income of $1.1 million. The change in fair value of the derivative liability was a loss in the amount of $86.2 million in 2020 as compared to a gain of $4.3 million during the year ended December 31, 2019 due changes in the underlying assumptions of the derivative liability, primarily related to an increase in our common stock price between December 31, 2020 and 2019. We expect the change in fair value of the derivative liability will continue to fluctuate until it is settled based on the extent changes occur in the underlying assumptions.

Liquidity and Capital Resources

Since inception, we have incurred significant operating losses. Our net losses were $155.6 million and $86.4 million, for the years ended December 31, 2020 and 2019, respectively. As of December 31, 2020, we had an accumulated deficit of $539.3 million.

We have generated limited revenue to date. In 2014, we began recognizing revenue from sales of ReSure Sealant. We commercially launched DEXTENZA for post-surgical ocular inflammation and pain in July 2019. All of our other sustained drug delivery products are in various phases of clinical and preclinical development. Our ability to generate product revenues sufficient to achieve profitability will depend heavily on our continued commercialization of DEXTENZA for the treatment of ocular inflammation and pain following ophthalmic surgery and our obtaining marketing approval for and commercializing other products with significant market potential, including DEXTENZA for the treatment of ocular itching associated with allergic conjunctivitis, OTX-TKI for wet AMD, OTX-TIC for glaucoma or ocular hypertension, and OTX-CSI and OTX-DED for dry eye disease. While it is difficult to predict the extent or duration of the impact of the global COVID-19 pandemic on future financial results, we anticipate current guidelines and recommendations from the global health authorities, including the delay of elective surgeries, will impact revenue in 2021.

Through December 31, 2020, we have financed our operations primarily through private placements of our preferred stock, public offerings of our common stock, private placements of our convertible notes and borrowings under credit facilities, which has resulted in net proceeds of $637.2 million to us. As described above, we issued and sold an aggregate of 21,949,841 shares of our common stock in the May 2020 Offering, the October 2020 Offering, and the December 2020 Offering. We received net proceeds from these offerings of approximately $210.0 million, after deducting underwriting discounts and commissions and offering expenses.

In April 2019, we entered into the 2019 Sales Agreement with Jefferies, acting as agent, for the issuance of up to $50.0 million of our common stock. Through March 1, 2021, we have sold 10,321,840 shares of common stock under the 2019 Sales Agreement, resulting in net proceeds of approximately $47.0 million after commissions and expenses. We have $1.3 million available for issuance as of March 1, 2021.

On March 2019, we issued $37.5 million of the 2026 Convertible Notes. The 2026 Convertible Notes accrue interest at an annual rate of 6% of its outstanding principal amount, payable in cash at maturity on March 1, 2026, unless earlier converted, repurchased or redeemed. The holders of the 2026 Convertible Notes may convert all or part of the outstanding principal amount of their 2026 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 2026 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, none of which have occurred to date.

In April 2014, we borrowed $15.0 million in aggregate principal amount under our Credit Facility and used $1.9 million of this amount to repay $1.7 million aggregate principal amount of indebtedness and pay $0.2 million of other amounts due in connection with our termination of a prior credit facility. In December 2015, we amended the Credit Agreement to increase the aggregate principal amount borrowed under our Credit Facility to $15.6 million, extend the interest-only payment period through December 2016, and extend the maturity date to December 1, 2019. In March 2017, we amended the Credit Agreement to increase the aggregate principal amount borrowed under our Credit Facility to $18.0 million and extend the interest only period through February 1, 2018 and extend the maturity date to February 1, 2020. In December 2018, we amended the Credit Agreement to increase the aggregate principal amount borrowed under our Credit Facility to $25.0 million, extend the interest-only payment period through December 2020 and extend the to maturity to date to December 2023. Amounts borrowed under the Credit Agreement are at a LIBOR base rate, subject to a 2.00% floor, plus 7.25%. As of December 31, 2020, the interest rate was 9.25%. In addition, a final payment (exit fee) equal to 3.5% of amounts drawn under the Credit Facility is due upon maturity. If we elect to prepay amounts borrowed under the Credit Agreement, we would also owe a prepayment fee of 2.00% of amounts prepaid until December 2021 or 1.00% of amounts prepaid thereafter. See "—Contractual Obligations and Commitments" for additional information.

As of December 31, 2020, we had cash and cash equivalents of $228.1 million, notes payable of $25.0 million face value and senior subordinated convertible notes of $37.5 million par value, plus accrued interest of $4.2 million.

Cash Flows

Based on our current plans and forecasted expenses, which includes estimates related to anticipated cash inflows from DEXTENZA and ReSure Sealant product sales and cash outflows from operating expenses, we believe that our existing cash and cash equivalents, as of December 31, 2020, will enable us to fund our planned operating expenses, debt service obligations and capital expenditure requirements through 2023. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect.

The following table summarizes our sources and uses of cash for each of the periods presented:

	Year Ended December 31,	
	2020	2019
	(in thousands)	
Cash used in operating activities	$ (53,554)	$ (77,578)
Cash used in investing activities	(841)	(2,238)
Cash provided by financing activities	228,014	75,341
Net increase in cash and cash equivalents	$ 173,620	$ (4,475)

Operating activities. Net cash used in operating activities was $53.6 million for the year ended December 31, 2020, primarily resulting from our net loss of $155.6 million, partially offset by non-cash charges of $100.9 million and cash provided by changes in our operating assets and liabilities of $1.1 million. Our net loss was primarily attributed to research and development activities, selling and marketing costs and our general and administrative expenses partially

offset by $17.4 million of revenue in the period. Our net non-cash charges during the year ended December 31, 2020 primarily consisted of the change in fair value of the derivative liability of $86.2 million, $7.5 million of stock-based compensation expense, $4.4 million of non-cash interest expense and $2.8 million of depreciation expense. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2020 consisted primarily of a $12.0 million in deferred revenue partially offset by the change in the working capital accounts and a $9.7 million increase in accounts receivable.

Net cash used in operating activities was $77.6 million for the year ended December 31, 2019, primarily resulting from our net loss of $86.4 million, partially offset by non-cash charges of $10.7 million and cash provided by changes in our operating assets and liabilities of $1.9 million. Our net loss was primarily attributed to research and development activities, selling and marketing costs and our general and administrative expenses partially offset by $4.2 million of revenue in the period. Our net non-cash charges during the year ended December 31, 2019 primarily consisted of $8.8 million of stock-based compensation expense, $2.5 million of depreciation expense and non-cash interest expense partially offset by the change in fair value of the derivative liability of $4.3 million. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2019 consisted primarily of a $1.7 million increase in accrued expenses and deferred rent and a $2.3 million increase in accounts receivable.

Investing activities. Net cash used in investing activities was $0.8 million for the year ended December 31, 2020, consisting of cash used to purchase property and equipment. Net cash used in investing activities was $2.2 million for the year ended December 31, 2019, consisting of cash used to purchase property and equipment.

Financing activities. Net cash provided by financing activities for 2020 was $228.0 million and consisted primarily of proceeds from the May 2020 Offering, the October 2020 Offering and the December 2020 Offering of an aggregate of $210.0 million, net of underwriting discounts and commissions and offering expenses; proceeds from sales under the 2019 Sales Agreement of $14.4 million, net of commissions and other offering expenses; proceeds from the exercise of stock options of $2.6 million; and proceeds from issuance of common stock pursuant to our employee stock purchase plan of $0.8 million.

Net cash provided by financing activities for 2019 was $75.3 million and consisted primarily of proceeds from the 2026 Convertible Notes of $37.3 million and the 2016 Sales Agreement of $4.9 million, net of commissions and other offering expenses and the 2019 Sales Agreement of $32.6 million, net of commissions and other offering expenses.

Funding Requirements

We expect to continue to incur losses in connection with our ongoing activities, particularly as we advance the clinical trials of our products in development and increase our sales and marketing resources to support the DEXTENZA launch 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 to commercialize DEXTENZA in the United States;
- continue to develop and expand our sales, marketing and distribution capabilities for DEXTENZA and any of our products or product candidates;
- continue to pursue the clinical development of DEXTENZA for additional indications;
- continue ongoing clinical trials of our product candidates OTX-TKI, OTX-TIC, OTX-CSI and OTX-DED;
- initiate planned Phase 2 clinical trials for our product candidates OTX-TKI and OTX-TIC;
- conduct joint research and development under our strategic collaboration with Regeneron, for the development and potential commercialization of products containing our extended-delivery hydrogel formulation in combination with Regeneron’s large molecule, VEGF-targeting compounds to treat retinal diseases;

- conduct research and development activities on, and seek regulatory approvals for, DEXTENZA and OTX-TIC in certain Asian countries 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, including through additional preclinical development activities associated with our front-of-the-eye and back-of-the-eye programs and potential opportunities outside the field of ophthalmology;
- 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, our ongoing 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 and management systems and personnel, including personnel to support our clinical development, manufacturing and commercialization efforts and our operations as a public company;
- defend ourselves against legal proceedings;
- 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.

Based on our current plans and forecasted expenses, which includes estimates related to anticipated cash inflows from DEXTENZA and ReSure Sealant product sales and cash outflows from operating expenses, we believe that our existing cash and cash equivalents, as of December 31, 2020, will enable us to fund our planned operating expenses, debt service obligations and capital expenditure requirements through 2023. We have based this estimate 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:

- our ability to continue to commercialize and sell DEXTENZA in the United States;
- the costs, timing and outcome of regulatory review of our product candidates by the FDA, the EMA or other regulatory authorities;
- the level of product sales from DEXTENZA and any additional products for which we obtain marketing approval in the future;
- the costs of manufacturing, sales, marketing, distribution and other commercialization efforts with respect to DEXTENZA and any additional products for which we obtain marketing approval in the future;

- the costs of expanding our facilities to accommodate our manufacturing needs and headcount;
- the progress, costs and outcome of our planned and ongoing clinical trials of our extended-delivery drug delivery product candidates, in particular DEXTENZA for additional indications, OTX-TIC for the treatment of glaucoma or ocular hypertension, OTX-TKI for the treatment of wet AMD, 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;
- the scope, progress, costs and outcome of preclinical development and clinical trials of our other product candidates;
- 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, from Regeneron as potential option exercise fees, development, regulatory and sales milestone payments and royalty payments and the amounts we are obligated to pay to Regeneron as reimbursement if it chooses to exercise its option to advance a product candidate under our collaboration agreement;
- the amounts we are entitled to receive, if any, from AffaMed 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 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, government or other third-party funding, collaborations, strategic alliances, licensing arrangements, royalty agreements, and marketing and distribution arrangements. We do not have any committed external source of funds, although our collaboration agreement with Regeneron provides for Regeneron's reimbursement of certain preclinical expenses incurred by us under our collaboration agreement and for our potential receipt of option exercise, development, regulatory and sales milestone payments and royalty payments and 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 as well as royalty payments. To the extent that we raise additional capital through the sale of equity or convertible debt securities, each security holder's ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect each security holder's rights as a common stockholder. 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. The covenants under our existing Credit Agreement, the pledge of our assets as collateral limit our ability to obtain additional debt financing. If we raise additional funds through government or other third-party funding, 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 or product candidates or grant licenses on terms that may not be favorable to us. In addition, the COVID-19 pandemic has already caused significant disruptions in the financial markets, and may continue to cause such disruptions, which could adversely impact our ability to raise additional funds through equity or debt financings. If we are unable to raise additional funds through equity or debt financings 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.

Since our inception in 2006, we have not recorded any U.S. federal or state income tax benefits for the net losses we have incurred in each year or our earned research and development tax credits, due to our uncertainty of realizing a benefit from those items. As of December 31, 2020, we had net operating loss, or NOL, carryforwards for federal and state income tax purposes of $354.7 million and $274.9 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 $229.1 million, can be carried forward indefinitely. As of December 31, 2020, we also had available research and development tax credit carryforwards for federal and state income tax purposes of $9.2 million and $5.0 million , respectively, which begin to expire in 2026 and 2025, respectively. We have not completed a study to assess whether an ownership change, generally defined as a greater than 50% change (by value) in the equity ownership of our corporate entity over a three-year period, has occurred or whether there have been multiple ownership changes since our inception, due to the significant costs and complexities associated with such studies. Accordingly, our ability to utilize our tax carryforwards may be limited. Additionally, U.S. tax laws limit the time during which these carryforwards may be utilized against future taxes. As a result, we may not be able to take full advantage of these carryforwards for federal and state tax purposes.

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	$ 12,770	$ 2,483	4,905	4,498	884
Credit Agreement	29,683	10,427	19,256	—	—
2026 Convertible Notes	53,475	—	—	53,475	—
Total	$ 95,928	$ 12,910	$ 24,161	$ 57,973	$ 884

The table above includes our enforceable and legally binding obligations and future commitments at December 31, 2020, 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, 2020. 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 and not included 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 July 2023, March 2024 and July 2027. We expect lease costs under these commitments to total $2.5 million in 2021 and increase annually. We expect total costs of approximately $12.8 million over the terms of our current leases.

Under our Credit Agreement, we have been permitted to make interest-only payments since December 2018. Commencing in January 2021, we are required to make 36 equal monthly installments of principal in the amount of $0.7 million, plus interest, through December 2023.

On March 2019, we issued the 2026 Convertible Notes pursuant to a note purchase agreement, or the Purchase Agreement, with Cap 1 LLC, an affiliate of Summer Road LLC. The 2026 Convertible Notes accrue interest at an annual rate of 6% of its outstanding principal amount, payable at maturity, on March 1, 2026, unless earlier converted, repurchased or redeemed. The holders of the 2026 Convertible Notes may convert all or part of the outstanding principal amount of their 2026 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 2026 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 2026 Convertible Note, we are obligated to make a cash payment to the holder of such 2026 Convertible Note for any interest accrued but unpaid on the principal amount converted. Upon the occurrence of a Corporate Transaction (as defined in the 2026 Convertible Notes), the holder of a 2026 Convertible Note is entitled, at such holder's option, to convert all of the outstanding principal amount of the 2026 Convertible Note in accordance with the foregoing and receive an additional, "make-whole" cash payment in accordance with a table set forth in each 2026 Convertible Note.

Upon the occurrence of a Corporate Transaction, each holder of a 2026 Convertible Note has the option to require us to repurchase all or part of the outstanding principal amount of such 2026 Convertible Note at a repurchase price equal to 100% of the outstanding principal amount of the 2026 Convertible Note to be repurchased, plus accrued and unpaid interest to, but excluding, the repurchase date.

On or after March 1, 2022, 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 2026 Convertible Notes, on a pro rata basis, at an optional redemption price equal to 100% of the outstanding principal amount of the 2026 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 2026 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.

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.

In October 2016, we entered into the Collaboration Agreement with Regeneron. If the Option is exercised, Regeneron will be obligated to conduct further preclinical development and an initial clinical trial under a collaboration plan. We are obligated to reimburse Regeneron for certain development costs during the period through the completion of the initial clinical trial, subject to a cap of $25.0 million, which cap may be increased by up to $5.0 million under certain circumstances. We have not included in the table above any payments to Regeneron under this Collaboration Agreement as the timing of such payments are not known. Regeneron will be responsible for funding an initial preclinical tolerability study, which Regeneron initiated in early 2018. We do not expect our funding requirements under our collaboration with Regeneron to be material over the next twelve months. If Regeneron elects to proceed with further development beyond the initial clinical trial, it will be solely responsible for conducting and funding further development and commercialization of product candidates. On May 8, 2020, we entered into an amendment (the "Regeneron Amendment") to the Collaboration Agreement. Pursuant to the Regeneron Amendment, we and Regeneron have adopted a new workplan to transition joint efforts under the Collaboration Agreement to the research and development of an extended-delivery formulation of aflibercept to be delivered to the suprachoroidal space. Regeneron has agreed to pay

our personnel and material costs for specified preclinical development activities in connection with the revised workplan, as well as certain other costs. In addition, the Regeneron Amendment provides for the modification of the terms of the Option previously granted to Regeneron under the Collaboration Agreement.

On October 29, 2020, we entered into the License Agreement with AffaMed. Pursuant to the terms of the License Agreement, we are generally responsible for expenses related to the development and commercialization of DEXTENZA regarding ocular inflammation and pain following cataract surgery and allergic conjunctivitis, or collectively, the DEXTENZA Field, and for OTX-TIC, or collectively with DEXTENZA, the AffaMed Licensed Products, regarding open-angle glaucoma and ocular hypertension, 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, 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.

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.

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.

Smaller Reporting Company Status

We are a "smaller reporting company," as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended. We would cease to be a smaller reporting company if we have a non-affiliate public float in excess of $250 million and annual revenues in excess of $100 million, or a non-affiliate public float in excess of $700 million, determined on an annual basis. As a smaller reporting company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not smaller reporting companies. These exemptions include:

- being permitted to provide only two years of audited consolidated financial statements in this Annual Report on Form 10-K, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- reduced disclosure obligations regarding executive compensation; and
- not being required to furnish a contractual obligations table in "Management's Discussion and Analysis of Financial Condition and Results of Operations"; and
- not being required to furnish a stock performance graph in our annual report.

We expect to continue to take advantage of some or all of the available exemptions as long as we continue to qualify as a smaller reporting company. We may cease to qualify as a smaller reporting company as early as June 30, 2021, which would require us to comply with disclosure requirements that are applicable to other public companies that are not smaller reporting companies following the filing of our Annual Report on Form 10-K for the year ending December 31, 2021, and any portions of our definitive proxy statement relating to our 2022 Annual Meeting of Stockholders incorporated by reference therein.

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, 2020, we had cash and cash equivalents of $228.1 million, which consisted of 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 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.

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-35 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, 2020. 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 Securities and Exchange Commission’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company’s management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2020, 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 the company. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) promulgated 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 Chief Executive Officer and Chief Financial Officer, assessed the effectiveness of our internal control over financial reporting as of December 31, 2020. 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, 2020, 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, 2020 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

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 2021 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 2021 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 2021 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 2021 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 Bruce Peacock is the “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 2021 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 2021 Annual Meeting of Stockholders and is incorporated in this Annual Report on Form 10-K by reference.

Securities Authorized for Issuance under Equity Compensation Plans

The information required by this item will be set forth in our Proxy Statement for the 2021 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 2021 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 2021 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	8-K	001-36554	7/30/2014	3.1	
3.2	Amended and Restated Bylaws 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	Description of Securities Registered under Section 12 of the Exchange Act	10-K	001-36554	3/12/2020	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	001-036554	11/12/2019	10.1	
10.9+	Amendment to 2019 Inducement Stock Incentive Plan					X
10.10+	Form of Non-statutory Stock Option Agreement under 2019 Inducement Stock Incentive Plan	10-Q	001-036554	11/12/2019	10.2	
10.11†	Amended and Restated License Agreement, dated January 27, 2012, between the Registrant and Incept LLC	S-1	333-196932	6/20/2014	10.8	

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
10.12	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	
10.13+	2014 Employee Stock Purchase Plan	S-1/A	333-196932	7/11/2014	10.10	
10.14	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	
10.15	Transition, Separation and Release of Claims Agreement by and between the Registrant and Dr. Amarpreet S. Sawhney dated as of May 29, 2019	8-K	001-36554	5/30/2019	10.1	
10.16	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	
10.17†	Collaboration, Option and License Agreement between the Registrant and Regeneron Pharmaceuticals, Inc. dated October 10, 2016	10-Q	001-36554	11/9/2016	10.1	
10.18	Open Market Sales Agreement℠, dated as of April 5, 2019, by and between the Registrant and Jefferies LLC	8-K	001-36554	4/5/2019	1.1	
10.19+	Employment Agreement, by and between the Registrant and Philip Strassburger, dated August 28, 2020					X
10.20	Consulting Agreement by and between the Registrant and Dr. Amarpreet S. Sawhney, dated as of May 29, 2019	8-K	001-36554	5/30/2019	10.2	
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+	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	
10.23+	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	
10.24	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	

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
10.25+	Employment Agreement, by and between the Registrant and Michael Goldstein, dated as of September 25, 2017	10-K	001-36554	3/8/2018	10.30	
10.26†	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	
10.27	Third Amended and Restated Credit and Security Agreement dated December 21, 2018 by and among MidCap Financial Trust, as administrative agent, the Registrant, and the Lenders listed therein	8-K	001-36554	12/28/2018	10.1	
10.28	First Amendment to Third Amended and Restated Credit and Security Agreement, dated as of February 21, 2019, by and among the Registrant, MidCap Financial Trust, as administrative agent, and the Lenders listed therein	8-K	001-36554	2/22/2019	10.3	
10.29	Second Amendment to Third Amended and Restated Credit and Security Agreement, by and among the Registrant, MidCap Financial Trust, as administrative agent, and the Lenders listed therein	10-Q	001-36554	8/7/2019	10.5	
10.30	Subordination Agreement, dated as of February 21, 2019, by and among the Registrant, MidCap Financial Trust, as administrative agent, and the Lenders listed therein	8-K	001-36554	2/22/2019	10.4	
10.31	Note Purchase Agreement (including Form of Senior Subordinated Convertible Note), 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	
10.32	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	
10.33+	Employment Agreement, by and between the Registrant and Patricia Kitchen, dated as of April 21, 2019	10-Q	001-36554	5/8/2020	10.1	

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
10.34*	Amendment to Collaboration, Option and License Agreement, by and between the Registrant and Regeneron, dated May 8, 2020	8-K	001-36554	5/14/2020	10.1	
10.35*	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	
10.36*	Supplement to License Agreement, by and between the Registrant and AffaMed Therapeutics Limited, dated as of January 18, 2021					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
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, 2021

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 and Chief Executive Officer (Principal Executive Officer)	March 11, 2021
/s/ Donald Notman Donald Notman	Chief Financial Officer (Principal Financial and Accounting Officer)	March 11, 2021
/s/ Charles Warden Charles Warden	Chairman of the Board	March 11, 2021
/s/ Jeffrey S. Heier, M.D. Jeffrey S. Heier, M.D.	Director	March 11, 2021
/s/ Seung Suh Hong, PH.D. Seung Suh Hong, PH.D.	Director	March 11, 2021
/s/ Richard L. Lindstrom, M.D. Richard L. Lindstrom, M.D.	Director	March 11, 2021
/s/ Bruce A. Peacock Bruce A. Peacock	Director	March 11, 2021
/s/ Leslie Williams Leslie Williams	Director	March 11, 2021

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 subsidiary (the "Company") as of December 31, 2020 and 2019, and the related consolidated statements of operations and comprehensive loss, of changes in stockholders' equity (deficit) and of cash flows for the years then ended, 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, 2020 and 2019, and the results of its operations and its cash flows for the years then ended 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 audit 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 Derivative Liability

As described in Note 4 to the consolidated financial statements, the Company's derivative liability balance was $98.3 million as of December 31, 2020 and the change in fair value recorded in other income (expense), net was expense of $86.2 million. The derivative liability was recorded at fair value upon the issuance of the 2026 convertible notes and is subsequently remeasured to fair value at each reporting period. The 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 derivative liability. The fair value of the 2026

convertible notes with and without the conversion option is estimated using a binomial lattice approach. The main inputs to valuing the 2026 convertible notes with the conversion option as of December 31, 2020 include the Company's stock price on the valuation date, the expected annual volatility of the Company's stock and the bond yield.

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 model; 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 the bond yield. 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 assumptions. Developing the independent estimate involved testing the completeness and accuracy of the inputs provided by management and evaluating management's assumptions related to bond yield based on observable market yield movements.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
March 11, 2021

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, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 228,057	$ 54,437
Accounts receivable, net	12,252	2,548
Inventory	1,201	954
Prepaid expenses and other current assets	4,650	2,231
Total current assets	246,160	60,170
Property and equipment, net	8,095	10,151
Restricted cash	1,764	1,764
Operating lease assets	5,844	6,655
Total assets	$ 261,863	$ 78,740
Liabilities and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 2,709	$ 3,268
Accrued expenses and other current liabilities	14,307	7,635
Operating lease liabilities	1,358	1,126
Notes payable, net of discount, current	8,290	—
Total current liabilities	26,664	12,029
Other liabilities:		
Operating lease liabilities, net of current portion	7,548	8,905
Derivative liability	98,313	12,124
Deferred revenue	12,000	—
Notes payable, net of discount	16,936	25,007
2026 convertible notes, net	24,307	24,305
Total liabilities	185,768	82,370
Commitments and contingencies (Note 15)		
Stockholders' equity (deficit):		
Preferred stock, $0.0001 par value; 5,000,000 shares authorized and no shares issued or outstanding at December 31, 2020 and December 31, 2019, respectively	—	—
Common stock, $0.0001 par value; 100,000,000 shares authorized and 75,996,732 and 50,333,559 shares issued and outstanding at December 31, 2020 and December 31, 2019, respectively	8	5
Additional paid-in capital	615,338	379,980
Accumulated deficit	(539,251)	(383,615)
Total stockholders' equity (deficit)	76,095	(3,630)
Total liabilities and stockholders' equity (deficit)	$ 261,863	$ 78,740

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,	
	2020	2019
Revenue:		
Product revenue, net	$ 17,403	$ 4,227
Total revenue, net	17,403	4,227
Costs and operating expenses:		
Cost of product revenue	2,083	2,325
Research and development	28,694	41,091
Selling and marketing	26,614	24,491
General and administrative	22,859	22,122
Total costs and operating expenses	80,250	90,029
Loss from operations	(62,847)	(85,802)
Other income (expense):		
Interest income	168	1,229
Interest expense	(6,768)	(6,101)
Change in fair value of derivative liability	(86,189)	4,310
Other income (expense), net	—	(8)
Total other income (expense), net	(92,789)	(570)
Net loss and comprehensive loss	$ (155,636)	$ (86,372)
Net loss per share, basic and diluted	$ (2.56)	$ (1.91)
Weighted average common shares outstanding, basic and diluted	60,752,225	45,273,231

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, 2018	41,518,091	$ 4	$ 333,114	$ (297,243)	$ 35,875
Issuance of common stock upon exercise of stock options	28,583	—	78	—	78
Issuance of common stock in connection with employee stock purchase plan	130,945	—	451	—	451
Issuance of common stock upon public offering, net of issuance costs	8,655,940	1	37,578	—	37,579
Stock-based compensation expense	—	—	8,759	—	8,759
Net loss	—	—	0	(86,372)	(86,372)
Balances at December 31, 2019	50,333,559	5	379,980	(383,615)	(3,630)
Issuance of common stock upon exercise of stock options	567,776	1	2,585		2,586
Issuance of common stock in connection with employee stock purchase plan	161,175	—	747		747
Issuance of common stock upon public offering, net of issuance costs	24,934,222	2	224,495		224,497
Stock-based compensation expense	—	—	7,531		7,531
Net loss	—	—		(155,636)	(155,636)
Balances at December 31, 2020	75,996,732	$ 8	$ 615,338	$ (539,251)	$ 76,095

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,	
	2020	**2019**
Cash flows from operating activities:		
Net loss	$ (155,636)	$ (86,372)
Adjustments to reconcile net loss to net cash used in operating activities		
Stock-based compensation expense	7,531	8,759
Non-cash interest expense	4,415	3,683
Change in fair value of derivative liability	86,189	(4,310)
Depreciation and amortization expense	2,773	2,530
Loss on disposal of property and equipment	—	7
Changes in operating assets and liabilities:		
Accounts receivable	(9,704)	(2,347)
Prepaid expenses and other current assets	(2,419)	(518)
Inventory	(247)	(737)
Operating lease assets	811	733
Accounts payable	(452)	124
Accrued expenses	2,311	1,714
Deferred revenue	12,000	—
Operating lease liabilities	(1,125)	(844)
Net cash used in operating activities	(53,554)	(77,578)
Cash flows from investing activities:		
Purchases of property and equipment	(841)	(2,238)
Net cash used in investing activities	(841)	(2,238)
Cash flows from financing activities:		
Proceeds from issuance of 2026 convertible notes, net of issuance costs	—	37,275
Proceeds from exercise of stock options	2,585	78
Proceeds from issuance of common stock pursuant to employee stock purchase plan	747	451
Proceeds from the Paycheck Protection Program Loan	3,201	—
Repayment of the Paycheck Protection Program Loan	(3,201)	—
Proceeds from issuance of common stock upon public offering, net	224,682	37,537
Net cash provided by financing activities	228,014	75,341
Net increase (decrease) in cash, cash equivalents and restricted cash	173,620	(4,475)
Cash, cash equivalents and restricted cash at beginning of period	56,201	60,676
Cash, cash equivalents and restricted cash at end of period	$ 229,821	$ 56,201
Supplemental disclosure of cash flow information:		
Cash paid for interest	$ 2,354	$ 2,298
Supplemental disclosure of non-cash investing and financing activities:		
Additional right of use asset and related lease liability	$ —	$ 2,044
Additions to property and equipment included in accounts payable and accrued expenses at balance sheet dates	$ 91	$ 214
Derivative liability in connection with issuance of 2026 convertible notes	$ —	$ 16,434
Public offering costs included in accounts payable and accrued expenses at balance sheet dates	$ 184	$ 42

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 focused on the formulation, development and commercialization of innovative therapies for diseases and conditions of the eye using its proprietary, bioresorbable hydrogel platform technology. The Company's product pipeline candidates provide differentiated drug delivery solutions that reduce the complexity and burden of the current standard of care by creating local programmed-release alternatives. Since inception, the Company's operations have been primarily focused on organizing and staffing the Company, acquiring rights to intellectual property, business planning, raising capital, developing its technology, identifying potential product candidates, undertaking preclinical studies and clinical trials, manufacturing initial quantities of its products and product candidates and building the initial sales and marketing infrastructure for the commercialization of the Company's approved products and product candidates and launching its initial product.

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.

As of December 31, 2020, the Company had two FDA-approved products in commercialization in the United States: DEXTENZA® (dexamethasone insert) 0.4mg, an intracanalicular insert for the treatment of post-surgical ocular inflammation and pain, and ReSure® Sealant, an ophthalmic device designed to prevent wound leaks in corneal incisions following cataract surgery. While ReSure Sealant is commercially available in the United States, it does not receive sales support and has not in the past generated, nor is it anticipated to in the future to generate, material revenues. The Company's other product candidates are in clinical stage 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, 2020, the Company had an accumulated deficit of $539,251. The Company believes that its existing cash and cash equivalents of $228,057, as of December 31, 2020, along with its current operating plan, which includes revenues from the sale of DEXTENZA, will enable it to fund its planned operating expenses, debt service obligations and capital expenditure requirements through at least the next 12 months. The future viability of the Company beyond that point is dependent on its 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 or other sources, which may include licensing, collaborations or other strategic transactions or arrangements. 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.

.

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP").

Risks and Uncertainties

The Company is monitoring the potential impact of the COVID-19 pandemic, if any, on the carrying value of certain assets. To date, the Company has not experienced a material business disruption, nor has it incurred impairment of any assets as a result of the COVID-19 pandemic. The extent to which these events may impact the Company's business will depend on future developments, which are highly uncertain and cannot be predicted at this time. The duration and intensity of the COVID-19 pandemic and any resulting disruption to the Company's operations is uncertain, and the Company will continue to assess the impact of the COVID-19 pandemic on its financial position.

2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The accompanying consolidated financial statements reflect the operations of the Company and its wholly-owned subsidiary. 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, revenue recognition, and the fair value of derivatives. 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 money market accounts, are stated at fair value.

Revenue Recognition

Product Revenue

The Company recognizes product revenue from DEXTENZA for the treatment of post-surgical ocular inflammation and pain, which it began selling to customers in June 2019, and ReSure Sealant. The Company has generated limited revenues from ReSure Sealant to date and does not expect significant future sales.

In November 2018, the FDA approved DEXTENZA for the treatment of ocular pain following ophthalmic surgery. The Company entered into a limited number of arrangements with specialty distributors in the United States to distribute DEXTENZA. The Company recognizes revenue in accordance with Accounting Standards Codification 606 – *Revenue from Contracts with Customers* ("Topic 606"). 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. The Company only applies 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 the Company will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the

scope of Topic 606, 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. For a complete discussion of accounting for product revenue, see Product Revenue, Net (below).

Product Revenue, Net— The Company derives its 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. In addition to distribution agreements with customers, the Company enters into arrangements with government payers that provide for government mandated 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). The Company has determined that the delivery of DEXTENZA to its 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. The Company has assessed the existence of a significant financing component in the agreements with its customers. The trade payment terms with the Company's customers do not exceed one year and therefore the Company has 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 the Company and its customers relating to the Company's 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 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 in certain circumstances as further discussed below. 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. The Company has received no returns to date and believes 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 the Company. 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 the Company 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 accounts receivables, net. Chargeback amounts are generally determined at the time of resale to the qualified government healthcare provider by 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 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.

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.

Rebates— The Company offers rebate payments for which ambulatory surgical centers, hospital out-patient departments and other prescribers qualify by meeting quarterly purchase volumes of DEXTENZA under the Company's rebate program. The Company calculates rebate payment amounts due under this program quarterly, based on actual qualifying purchase and applies a contractual discount rate. The calculation of the accrual for rebates is based on an estimate of claims 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.

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 payers. 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

To determine the appropriate amount of revenue to be recognized for arrangements the Company determines are within the scope of Topic 606, the Company performs the following steps: (i) identify the contract(s) with its 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 each performance obligation is satisfied.

The Company accounts for a contract with a customer that is within the scope of Topic 606 when all of the following criteria are met: (i) the arrangement has been approved by the parties and the parties are committed to perform their respective obligations; (ii) each party's rights regarding the goods and/or services to be transferred can be identified; (iii) the payment terms for the goods and/or services to be transferred can be identified; (iv) the arrangement has commercial substance; and (v) collection of substantially all of the consideration to which the Company will be entitled in exchange for the goods and/or services that will be transferred to the customer is probable. The Company also

determines the term of the contract based on the period in which the Company and its customer have present and enforceable rights and obligations for purposes of identifying the performance obligations and determining the transaction price.

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 transaction price is generally comprised of an upfront payment due at contract inception and variable consideration in the form of payments for the Company's goods and services and materials and milestone payments due upon the achievement of specified events. Other payments the Company could be entitled to include tiered royalties earned when customers recognize net sales of licensed products. The Company considers the existence of any significant financing component within its arrangements and have determined that a significant financing component does not exist in its arrangements as substantive business purposes exist 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 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, adjust 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.

The Company recognizes as an asset the incremental costs of obtaining a contract with a customer if the costs are expected to be recovered. The Company has elected a practical expedient wherein it recognizes the incremental costs of obtaining a contract as an expense when incurred if the amortization period of the asset that it otherwise would have recognized is one year or less. To date, the Company has not incurred any incremental costs of obtaining a contract with a customer.

Inventory

The Company values its inventories at the lower of cost or estimated net realizable value. The Company determines the cost of its inventories, which includes amounts related to materials and manufacturing overhead, on a first-in, first-out basis. 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 determination of whether inventory costs will be realizable requires estimates by management. If actual market conditions are less favorable than projected by management, additional write-downs of inventory may be required, which would be recorded as a cost of product revenue in the consolidated statements of operations and comprehensive loss.

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.

Inventory consisted of the following:

	December 31,	
	2020	2019
Raw materials	$ 384	$ 217
Work-in-process	232	148
Finished goods	585	589
	$ 1,201	$ 954

Restricted Cash

As of December 31, 2020 and 2019, the Company held restricted cash of $1,764, respectively, on its consolidated balance sheet. The Company held restricted cash as security deposits for the lease of its manufacturing space and corporate headquarters.

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, 2020	December 31, 2019
Cash and cash equivalents	$ 228,057	$ 54,437
Restricted cash	1,764	1,764
Total cash, cash equivalents and restricted cash as shown on the statements of cash flows	$ 229,821	$ 56,201

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 all cash and cash equivalents balances at one accredited financial institution, 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 sales of its product sales could be adversely affected by a significant interruption in the supply of any of the components of these products.

For the year ended December 31, 2020, three specialty distributor customers accounted for 42%, 29% and 12% of the Company's total revenue and three specialty distributor customers accounted for 45%, 33% and 15% of the

Company's total accounts receivable. No other customer accounted for more than 10% of total revenue or accounts receivable for the year ended December 31, 2020.

For the year ended December 31, 2019, two specialty distributor customers accounted for 27% and 11% of the Company's total revenue and three specialty distributor customers accounted for 39%, 18% and 11% of the Company's total accounts receivable. No other customer accounted for more than 10% of total revenue or accounts receivable for the year ended December 31, 2019.

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.

The Company's cash equivalents at December 31, 2020 and 2019 were carried at fair value determined according to the fair value hierarchy described above (Note 3). The Company's derivative liability at December 31, 2020 and 2019 was carried at fair value determined according to the fair value hierarchy described above and classified as a Level 3 measurement. 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 notes payable (Note 9) are recorded at amortized costs, which approximates fair value due to their short-term nature.

On March 1, 2019, the Company issued $37,500 aggregate principal amount of unsecured senior subordinated convertible notes (the "2026 Convertible Notes") (Note 5) which is carried, net of derivative liability, at its amortized cost of $24,307 at December 31, 2020. The estimated fair value of the 2026 Convertible Notes was $129,362 and $36,849 at December 31, 2020 and 2019. The fair value of the 2026 Convertible Notes was estimated utilizing a binomial lattice model which requires the use of Level 3 unobservable inputs. 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.

Derivative Liability

The 2026 Convertible Notes allow the holders to convert all or part of the outstanding principal of their 2026 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 2026 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 Company measures the value of the embedded conversion option at its estimated fair value and recognizes 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 the Company's consolidated balance sheet.

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.

Impairment of Long-Lived Assets

Long-lived assets consist of property and equipment. 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.

Research Contract Costs and Accruals

The Company has entered into various research and development contracts with research institutions and other companies both inside and outside of the United States. Certain of these agreements have cancellation clauses, and related payments are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research 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 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.

Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are recorded as general and administrative expenses as incurred, as recoverability of such expenditures is uncertain.

Accounting for Stock-Based Compensation

The Company measures all stock options and other stock-based awards granted to employees and directors at the fair value on the date of the grant using the Black-Scholes option-pricing model. 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.

Following the Company's adoption of Accounting Standards Update ("ASU") 2018-07, Compensation—Stock Compensation (Topic 718), Improvements to Nonemployee Share-Based Payment Accounting ("ASU 2018-07"), on January 1, 2019, for stock-based awards issued to non-employees, the Company no longer revalues non-employee awards at each reporting date and instead calculates the fair value of the awards as of the grant date using the Black-Scholes option-pricing model. Compensation expense for these awards is recognized over the related service period.

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.

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.

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 as well as the related net interest and penalties.

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 tangible assets are held in the United States. Revenue to date has been generated through product sales, all of which has been earned in the United States.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with stockholders. For the years ended December 31, 2020 and 2019, 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, including the assumed conversion of the Company's 2026 Convertible Notes, 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 the 2026 Convertible Notes, 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 the 2026 Convertible Notes (which includes amortization of the discount created upon bifurcation of the conversion option from the debt) and, the mark-to-market gain or loss each period to the bifurcated conversion option, if the impact was not anti-dilutive.

Recently Adopted Accounting Pronouncements

In August 2018, the FASB issued ASU No. 2018-13, Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement ("ASU 2018-13"), which modifies the existing disclosure requirements for fair value measurements. The new disclosure requirements include disclosure related to changes in unrealized gains or losses included in other comprehensive income (loss) for recurring Level 3 fair value measurements held at the end of each reporting period and the explicit requirement to disclose the range and weighted average of significant unobservable inputs used for Level 3 fair value measurements. The other provisions of ASU 2018-13 include eliminated and modified disclosure requirements.

In November 2018, the FASB issued ASU No. 2018-18, Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606 ("ASU 2018-18"). ASU 2018-18 makes targeted improvements to GAAP for collaborative arrangements, including (i) clarification that certain transactions between collaborative arrangement participants should be accounted for as revenue under ASC 606 when the collaborative arrangement participant is a customer in the context of a unit of account, (ii) adding unit-of-account guidance in ASC 808, Collaborative Arrangements, to align with the guidance in ASC 606 and (iii) a requirement that in a transaction with a collaborative arrangement participant that is not directly related to sales to third parties, presenting the transaction together with revenue recognized under ASC 606 is precluded if the collaborative arrangement participant is not a customer. The Company adopted this pronouncement as required effective January 1, 2020 and its adoption did not have a material impact on the Company's consolidated financial statements.

Recently Issued Accounting Pronouncements

In December 2019, the FASB issued ASU No. 2019-12, Income Taxes Topic 740, Simplifying the Accounting for Income Taxes ("ASU 2019-12"). ASU 2019-12 removes certain exceptions for investments, intra-period allocations and interim calculations, and adds guidance to reduce complexity in accounting for income taxes. The guidance is effective for fiscal years beginning after December 15, 2020, including interim periods within those fiscal years. The Company is currently evaluating the impact that the adoption of ASU 2019-12 will have on its consolidated financial statements.

In June 2016, the FASB issued ASU No. 2016-13, Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments (''ASU 2016-13''), which requires the measurement and recognition of expected credit losses for financial assets held at amortized cost. ASU 2016-13 replaces the existing incurred loss impairment model with an expected loss model. It also eliminates the concept of other-than-temporary impairment and requires credit losses related to available-for-sale debt securities to be recorded through an allowance for credit losses rather than as a reduction in the amortized cost basis of the securities. These changes may result in earlier recognition of credit losses. In November 2018, the FASB issued ASU No. 2018-19, Codification Improvements to Topic 326, Financial Instruments—Credit Losses, which narrowed the scope and changed the effective date for non-public entities for ASU 2016-13. The FASB subsequently issued supplemental guidance within ASU No. 2019-05, Financial Instruments—Credit Losses (Topic 326): Targeted Transition Relief (''ASU 2019-05''). ASU 2019-05 provides an option to irrevocably elect the fair value option for certain financial assets previously measured at amortized cost basis. For public entities that are Securities and Exchange Commission filers, excluding entities eligible to be smaller reporting companies, ASU 2016-13 is effective for annual periods beginning after December 15, 2019, including interim periods within those fiscal years. For all other entities, ASU 2016-13 is effective for annual periods beginning after December 15, 2022, including interim periods within those fiscal years. Early adoption is permitted. This standard will be effective for the Company on January 1, 2023. The Company is currently evaluating the potential impact that this standard may have on its consolidated financial statements and related disclosures.

In August 2020, the FASB issued ASU No. 2020-06, Debt – Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40) ("ASU 2020-06"). This standard amends the guidance on convertible instruments and the derivatives scope exception for contracts in an entity's own equity and improves and amends the related earnings per share guidance for both Subtopics. The amendments in the ASU are effective for public business entities that meet the definition of an SEC filer, excluding entities eligible to be smaller reporting companies as defined by the SEC, for fiscal years beginning after December 15, 2021, including interim periods within those fiscal years. Early adoption is permitted, but no earlier than fiscal years beginning after December 15, 2020, including interim periods within those fiscal years. The FASB also specified that an entity should adopt the guidance as of the beginning of its fiscal year and is not permitted to adopt the guidance in an interim period. The Company is assessing the potential impact of ASU 2020-06 on its consolidated financial statements.

3. 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, 2020 and 2019 and indicate the level of the fair value hierarchy utilized to determine such fair value:

	Fair Value Measurements as of December 31, 2020 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ 213,372	$ —	$ —	$ 213,372
Liability:				
Derivative liability (Note 4)	—	—	98,313	98,313
Total	$ 213,372	$ —	$ 98,313	$ 311,685

	Fair Value Measurements as of December 31, 2019 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ —	$ 45,156	$ —	$ 45,156
Liability:				
Derivative liability (Note 4)	—	—	12,124	12,124
Total	$ —	$ 45,156	$ 12,124	$ 57,280

During the year ended December 31, 2020 and 2019, there were no transfers between Level 1 and 2.

4. Derivative Liability

The 2026 Convertible Notes (Note 5) contained an embedded conversion option that met the criteria to be bifurcated and accounted for separately from the 2026 Convertible Notes (the "Derivative Liability"). The Derivative Liability was recorded at fair value upon the issuance of the 2026 Convertible Notes and is subsequently remeasured to fair value at each reporting period. The 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 Derivative Liability.

The fair value of the 2026 Convertible Notes with and without the conversion option is estimated using a binomial lattice approach. The main inputs to valuing the 2026 Convertible Notes with the conversion option are as follows:

	As of	
	December 31, 2020	December 31, 2019
Company's stock price	$ 20.70	$ 3.95
Expected annual volatility	105.5 %	85.8 %
Bond yield	12.0 %	13.0 %

The bond yield was derived by making the fair value of the 2026 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.

A roll forward of the derivative liability is as follows:

	As of
Balance at December 31, 2018	$ —
Initial value	16,434
Change in fair value	(4,310)
Balance at December 31, 2019	$ 12,124
Change in fair value	86,189
Balance at December 31, 2020	$ 98,313

5. Convertible Notes

On March 1, 2019, the Company issued $37,500 of 2026 Convertible Notes. Each 2026 Convertible Note accrues interest at an annual rate of 6% of its outstanding principal amount, which is payable, along with the principal amount at maturity, on March 1, 2026, unless earlier converted, repurchased or redeemed. The Company presents deferred 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 2026 Convertible Notes was 14.8% through December 31, 2020.

The holders of the 2026 Convertible Notes may convert all or part of the outstanding principal amount of their 2026 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 2026 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.

At its election, the Company may choose to make such conversion payment in cash, in shares of common stock, or a combination thereof. Upon any conversion of any 2026 Convertible Note, the Company is obligated to make a cash payment to the holder of such 2026 Convertible Note for any interest accrued but unpaid on the principal amount converted. Upon the occurrence of a Corporate Transaction (as defined below), each holder has the option to require the Company to repurchase all or part of the outstanding principal amount of such note at a repurchase price equal to 100% of the outstanding principal amount of the 2026 Convertible Note to be repurchased, plus accrued and unpaid interest to, but excluding the repurchase date. In addition, each holder is entitled to receive an additional make-whole cash payment in accordance with a table set forth in each 2026 Convertible Note.

Upon conversion by the holder, the Company has the right to select the settlement of the conversion in either shares of common stock, cash, or in a combination thereof. In addition, the Company is obligated to make a cash

payment to the holder of such 2026 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 2026 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 2026 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 2026 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 2026 Convertible Note to, but excluding, the corporate transaction conversion date (to the extent such date occurs prior to March 1, 2026, the maturity date of the 2026 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 2026 Convertible Note at a repurchase price equal to 100% of the outstanding principal amount of the 2026 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").

On or after March 1, 2022, 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 2026 Convertible Notes, on a pro rata basis, at an optional redemption price equal to 100% of the outstanding principal amount of the 2026 Convertible Notes to be redeemed, plus accrued and unpaid interest to, but excluding, the optional redemption date.

The 2026 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.

As discussed in Note 4, the Company determined that the embedded conversion option is required to be separated from the 2026 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 2026 Convertible Notes. The

Company is amortizing the discount to interest expense over the term of the 2026 Convertible Notes using the effective interest method.

A summary of the 2026 Convertible Notes at December 31, 2020 and 2019 is as follows:

	December 31, 2020	December 31, 2019
2026 Convertible Notes	$ 37,500	$ 37,500
Less: unamortized discount	(13,193)	(15,101)
Total	$ 24,307	$ 22,399
Accrued interest	—	1,906
Total	$ 24,307	$ 24,305

6. Property and Equipment, net

Property and equipment, net consisted of the following:

	December 31, 2020	December 31, 2019
Equipment	$ 10,186	$ 9,511
Leasehold improvements	9,074	9,074
Furniture and fixtures	1,281	1,132
Software	220	214
Construction in progress	120	239
	20,881	20,170
Less: Accumulated depreciation and amortization	(12,786)	(10,019)
	$ 8,095	$ 10,151

Depreciation and amortization expense was $2,773 and $2,530 for the years ended December 31, 2020 and 2019, respectively.

7. Accrued Expenses

Accrued expenses consisted of the following:

	December 31, 2020	December 31, 2019
Accrued payroll and related expenses	$ 5,853	$ 5,042
Accrued rebates and programs	1,438	175
Accrued professional fees	868	1,011
Accrued research and development expenses	1,013	849
Accrued interest payable on 2026 convertible notes	4,194	—
Accrued other	941	558
	$ 14,307	$ 7,635

8. Collaboration Agreements

AffaMed License Agreement

On October 29, 2020, the Company entered into 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 OTX-TIC product candidate (collectively with DEXTENZA, the “AffaMed Licensed Products”) regarding open-angle glaucoma and 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. The Company is also eligible to receive up to an additional $91,000 in aggregate, inclusive of a low-seven-figure clinical support payment, 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 OTX-TIC 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 license, regulatory filings and manufacturing for the Company’s OTX-TIC product candidate regarding open-angle glaucoma and ocular hypertension in the Territories;
- obligations to participate on various joint research, development and project committees; and
- the conduct of a Phase 2 clinical trial of OTX-TIC

The Company has concluded there is a combined performance obligation for a development and commercialization license and manufacturing obligations for DEXTENZA Field and the Company’s OTX-TIC product candidate regarding open-angle glaucoma and ocular hypertension in the Territories.

Further, AffaMed cannot exploit the value of the development and commercialization license for DEXTENZA Field and the Company’s OTX-TIC product candidate regarding open-angle glaucoma and ocular hypertension in the

Territories without receipt of supply as the development and commercialization license does not convey to AffaMed the right to manufacture and therefore the Company has combined the development and commercialization license and the manufacturing obligations into one performance obligation.

The Company has concluded that the right of AffaMed to opt into the Global Studies for DEXTENZA and OTX-TIC are options that do not convey a material right to AffaMed. Therefore, these have not been recognized as performance obligations upon the inception of the License Agreement.

With respect to the obligation of the Company to participate in joint research, development and project committees the Company has concluded that these obligations are not material.

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 obligation, 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, 2020, the transaction price was determined to be $12,000. All potential regulatory, development and commercial milestone payments in the amount of $91,000 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, 2020. 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 combined performance obligations for DEXTENZA Field and the Company's OTX-TIC product candidate 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 has not recognized any revenue under the License Agreement as of December 31, 2020 as there has not been any delivery of product under the License Agreement. The Company does not expect to recognize material revenue from the License Agreement in 2021. The entire transaction price is recorded as deferred revenue as of December 31, 2020.

Regeneron Collaboration Agreement

On October 10, 2016, the Company entered into a Collaboration, Option and License Agreement (the "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. The Collaboration Agreement does not cover the development of any product candidates that deliver small molecule drugs, including TKIs for any target including VEGF, or any product candidate that delivers large molecule drugs other than those that target VEGF proteins.

Under the terms of the Collaboration Agreement, the Company and Regeneron have 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 has 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 is responsible for funding an initial preclinical tolerability study.

If Regeneron decided to exercise the Option, Regeneron will be obligated to conduct further preclinical development and an initial clinical trial under a collaboration plan. The Company is obligated to reimburse Regeneron for certain development costs incurred by Regeneron under the collaboration plan during the period through the completion of the initial clinical trial, subject to a cap of $25,000, which cap may be increased by up to $5,000 under certain circumstances. If Regeneron elects to proceed with further development following the completion of the collaboration plan, it will be solely responsible for conducting and funding further development and commercialization of product candidates. If the Option is exercised, Regeneron is required to use commercially reasonable efforts to research, develop and commercialize at least one Licensed Product. Such efforts shall include initiating the dosing phase of a subsequent clinical trial within specified time periods following the completion of the first-in-human clinical trial or the initiation of preclinical toxicology studies, subject to certain extensions.

Under the terms of the Collaboration Agreement, Regeneron has agreed to pay the Company $10,000 upon the exercise of the Option. The Company is also eligible to receive up to $145,000 per Licensed Product upon the achievement of specified development and regulatory milestones, $100,000 per Licensed Product upon first commercial sale of such Licensed Product and up to $50,000 based on the achievement of specified sales milestones for all Licensed Products. In addition, the Company is entitled to tiered, escalating royalties, in a range from a high-single digit to a low-to-mid teen percentage of net sales of Licensed Products.

In December 2017, the Company delivered to Regeneron a proposed final formulation for the initial preclinical tolerability study. Regeneron initiated the preclinical study in early 2018. The Company and Regeneron subsequently reached an understanding that the proposed formulation was not final and ceased development of it.

On May 8, 2020, the Company entered into an amendment (the "Regeneron Amendment") to the Collaboration Agreement. Pursuant to the Regeneron Amendment, the Company and Regeneron have adopted a new work plan to transition joint efforts under the Collaboration Agreement to the research and development of an extended-delivery formulation of aflibercept to be delivered to the suprachoroidal space. Regeneron has 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 provides for the modification of the terms of the Option previously granted to Regeneron under the Collaboration Agreement. As amended, the Option is exclusive for twenty-four months following May 8, 2020. Through December 31, 2020, the Option has not been exercised, and no payments have been made.

As of December 31, 2020, the Company has recorded $1,256 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, 2020, the Company has included the $1,256 in prepaid expenses and other current assets.

9. Notes Payable

The Company entered into a credit and security agreement in 2014 (as amended to date, the "Credit Agreement") establishing the Company's credit facility (the "Credit Facility"). The Company has a total borrowing capacity of $25,000 under the Credit Facility, which was fully drawn down as of December 31, 2020.

In December 2018, the Company amended the terms of the Credit Agreement to increase total indebtedness under the Credit Facility to $25,000 which was used primarily to pay-off outstanding balances as of the closing date. The Company was required to make interest-only payments under the Credit Facility until December 2020. Commencing in January 2021, the Company is required to make 36 equal monthly installments of principal in the amount of $694, plus interest, through December 2023.

Amounts borrowed under the Credit Agreement are at LIBOR base rate, subject to 2.00% floor, plus 7.25%. The interest rate on the date of the amendment was 9.76%. As of December 31, 2020, the interest rate was 9.25%. In addition, a final payment (exit fee) equal to 3.5% of amounts drawn under the Credit Facility, or $875 based on

borrowings of $25,000, is due upon the maturity date of December 21, 2023. The Company is accruing the exit fee through December 21, 2023.

On August 2, 2019, the Company entered into a second amendment to the Credit Agreement in which the lenders agreed to remove the financial covenant requiring the Company to maintain a minimum of $5,000 of cash on hand. Prior to this amendment, the Company was required to maintain a minimum of $5,000 of cash on hand as a financial covenant to the borrowing arrangement, which the Company had included in long-term restricted cash.

There are no other financial covenants associated with the Credit Agreement. However, there are negative covenants restricting the Company's activities, including limitations on dispositions, mergers or acquisitions; encumbering its intellectual property; incurring indebtedness or liens; paying dividends; making certain investments; and engaging in certain other business transactions. As of December 31, 2020, the Company is not in violation of any of the covenants. The obligations under the Credit Agreement are subject to acceleration upon the occurrence of specified events of default, including a material adverse change in the Company's business, operations or financial or other condition. The debt is collateralized by substantially all of the Company's assets, including its intellectual property.

In accordance with the Credit Agreement, in connection with the Company's desire to issue and sell the 2026 Convertible Notes, the Company amended the terms of its debt with existing lenders in February 2019. The amendment added to the Credit Agreement, among other provisions, a negative covenant restricting the Company from paying the holders of the 2026 Convertible Notes ahead in priority to the existing lenders, for so long as indebtedness remains outstanding under the Credit Facility, and a cross-default provision to establish that an event of default under the purchase agreement for the 2026 Convertible Notes also constitutes an event of default under the Credit Agreement.

Borrowings outstanding are as follows:

	December 31, 2020	December 31, 2019
Borrowings outstanding	$ 25,000	$ 25,000
Accrued exit fee	355	180
Unamortized discount	(129)	(173)
	25,226	25,007
Less: current portion	(8,290)	—
Long-term notes payable	$ 16,936	$ 25,007

As of December 31, 2020, the annual repayment requirements for the Credit Facility, inclusive the final payment of $875 due at expiration, were as follows:

Year Ending December 31,	Principal	Final Payment	Total
2021	8,333	—	8,333
2022	8,333	—	8,333
2023	8,334	875	9,209
	$ 25,000	$ 875	$ 25,875

10. 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 and 2019 at a weighted average exercise price of $7.92 per share and an expiration date of April 17, 2021.

11. 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, 2020 and 2019.

12. 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.

On December 14, 2020, the Company entered into an underwriting agreement with Jefferies LLC ("Jefferies") and Piper Sandler & Co. (collectively with Jefferies, "the Underwriters") in connection with an underwritten public offering of 3,725,000 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 558,750 shares of common stock at the public offering price, less the underwriting discounts and commissions. The Underwriters subsequently exercised this option to purchase such option shares in full. The public offering price of the shares in this offering was $21.50 per share, and the Underwriters purchased all of the shares from the Company at a price of $20.21 per share. After deducting underwriting discounts and commissions and offering expenses, the Company received net proceeds from the offering of $86,390.

On October 13, 2020, the Company entered into an underwriting agreement with the Underwriters, in connection with an underwritten public offering of 7,180,000 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 1,077,000 shares of common stock at the public offering price, less the underwriting discounts and commissions. The Underwriters subsequently exercised this option to purchase such option shares in full. The public offering price of the shares in this offering was $9.75 per share, and the Underwriters purchased all of the shares from the Company at a price of $9.17 per share. After deducting underwriting discounts and commissions and offering expenses, the Company received net proceeds from the offering of $75,406.

In May 2020, the Company entered into an underwriting agreement with the Underwriters, in connection with an underwritten public offering of 8,181,819 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 1,227,272 shares of common stock at the public offering price, less the underwriting discounts and commissions. The Underwriters subsequently exercised this option to purchase such option shares in full. The public offering price of the shares in this offering was $5.50 per share, and the Underwriters purchased all of the shares from the Company at a price of $5.17 per share. After deducting underwriting discounts and commissions and offering expenses, the Company received net proceeds from the offering of $48,327.

On April 5, 2019, the Company entered into an Open Market Sales Agreement℠ (the "2019 Sales Agreement") with 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. In the twelve months ended December 31, 2019, the Company sold 7,337,459 shares of common stock under the 2019 Sales Agreement, resulting in net proceeds of approximately $32,626, respectively, after commissions and expenses. In the twelve months ended December 31, 2020, the Company sold 2,984,381 shares of common stock under the 2019 Sales Agreement, resulting in net proceeds of approximately $14,359, respectively, after commissions and expenses. From inception through March 1, 2021, the Company sold an aggregate of 10,321,840 shares of common stock under the 2019 Sales Agreement, resulting in net proceeds of approximately $46,985 after commissions and expenses. The Company has $1,326 available for issuance as of March 1, 2021.

In November 2016, the Company entered into a controlled equity offering sales agreement, (the "2016 Sales Agreement") with Cantor Fitzgerald & Co., ("Cantor"), under which the Company may offer and sell its common stock having aggregate proceeds of up to $40,000 may be sold from time to time. During the year ended December 31, 2018, the Company sold 4,121,173 shares of common stock under the 2016 Sales Agreement, resulting in net proceeds of approximately $26,824 after underwriting discounts, commissions and expenses. Through December 31, 2018, the Company had sold 5,011,741 shares of common stock under the 2016 Sales Agreement, resulting in net proceeds of

approximately $33,427 after underwriting discounts, commissions and expenses. In the three months ended March 31, 2019, the Company sold 1,318,481 shares of common stock under the 2016 Sales Agreement, resulting in net proceeds of approximately $4,954 after underwriting discounts and commissions and expenses. As of February 25, 2019, the Company had no amounts remaining available for future sale under the 2016 Sales Agreement. On February 28, 2019, pursuant to the 2016 Sales Agreement, the Company delivered a termination notice to Cantor, terminating the 2016 Sales Agreement. Through March 31, 2019, the Company sold 6,330,222 shares of common stock under the 2016 Sales Agreement, resulting in net proceeds of approximately $38,381 after underwriting discounts and commissions and expenses.

As of December 31, 2020, the Company had reserved 11,191,284 shares of common stock for the exercise of outstanding stock options and the number of shares remaining available for grant under the Company's 2014 Stock Incentive Plan (the "2014 Plan") and the 2019 Inducement Stock Incentive Plan (the "2019 Inducement Plan"), the number of shares available for issuance under the 2014 Employee Stock Purchase Plan (Note 13), and the outstanding warrants to purchase common stock (Note 10).

13. Stock-Based Awards

2014 Stock Incentive Plan

The 2014 Plan provides for the grant of incentive stock options, non-statutory stock options, restricted stock awards, restricted stock units, stock appreciation rights and other stock-based awards. The number of shares initially reserved for issuance under the 2014 Plan was 1,336,907 shares of common stock, which was increased to 2,126,907 on January 1, 2015. The number of shares reserved for issuance may be increased by the number of shares under the 2006 Stock Option Plan (the "2006 Plan") that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company. The number of shares of common stock that may be issued under the 2014 Plan is subject to increase on the first day of each fiscal year, beginning on January 1, 2015 and ending on December 31, 2024, equal to the least of 1,659,218 shares of the Company's common stock, 4% 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, 2020, the number of shares available for issuance under the 2014 Plan increased by 1,659,218. As of December 31, 2020, 883,416 shares remained available for issuance under the 2014 Plan.

As required by the 2006 Plan and 2014 Plan, the exercise price for stock options granted is not to be less than the fair value of common shares as of the date of grant.

Inducement Stock Option Awards

On June 20, 2017, the Company issued to Antony Mattessich, who became a director of the Company on June 20, 2017 and the Company's President and Chief Executive Officer on July 26, 2017, a non-statutory stock option to purchase an aggregate of 590,000 shares of the Company's common stock at an exercise price of $10.94 per share. Subject to Mr. Mattessich's continued service to the Company, the stock option will vest over a four-year period, with 25% of the shares underlying the option award vesting on the one year anniversary of the grant date and the remaining 75% of the shares underlying the award vesting monthly thereafter. The stock option was issued outside of the Company's 2014 Plan as an inducement material to Mr. Mattessich's acceptance of an offer of employment with the Company in accordance with Nasdaq Listing Rule 5635(c)(4).

On July 9, 2019, the Company issued to the Senior Vice President, Head of Business Development, a non-statutory stock option to purchase an aggregate of 60,000 shares of its common stock at an exercise price of $5.13 per share. Subject to his continued service to the Company, the stock option will vest over a four-year period, with 25% of the shares underlying the option award vesting on the one-year anniversary of the grant date and the remaining 75% of the shares underlying the award vesting monthly thereafter. The stock option was issued outside of the Company's 2014 Plan as an inducement material to the individual's acceptance of an offer of employment with the Company in accordance with Nasdaq Listing Rule 5635(c)(4).

On October 29, 2019, the 2019 Inducement Plan was approved by the Board of Directors of the Company. 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, 2020, 650,000 shares remained available for issuance under the 2019 Inducement Plan.

2014 Employee Stock Purchase Plan

The Company's has a 2014 Employee Stock Purchase Plan (the "ESPP") with a total of 207,402 shares of common stock reserved for issuance under this plan which increased to 232,402 shares of common stock on January 1, 2015. 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, 2020, the number of shares available for issuance under the ESPP increased by 207,402. As of December 31, 2020, 524,194 shares of common stock remained available for issuance.

Stock Option Valuation

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 utilized the simplified method because the Company did 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.

As of December 31, 2020, there were no outstanding unvested service-based stock options held by nonemployees.

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,	
	2020	2019
Risk-free interest rate	1.12 %	2.25 %
Expected term (in years)	6	6
Expected volatility	86 %	87 %
Expected dividend yield	— %	— %

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, 2019	7,920,417	$ 6.67	7.6	$ 704
Granted	2,449,950	5.93		
Exercised	(567,776)	4.55		
Forfeited	(687,856)	5.84		
Outstanding as of December 31, 2020	9,114,735	$ 6.66	7.4	131,032
Options vested and expected to vest as of December 31, 2020	8,420,281	$ 6.78	7.2	120,315
Options exercisable as of December 31, 2020	5,001,463	$ 7.72	6.3	67,984

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 $4,307 and $54 during the years ended December 31, 2020 and 2019, respectively.

The weighted average grant date fair value of stock options granted to employees and directors during the years ended December 31, 2020 and 2019 was $5.93 and $2.99 per share, respectively.

Stock-based Compensation

The Company recorded stock-based compensation expense related to stock options in the following expense categories of its statements of operations:

	Year Ended December 31, 2020	2019
Research and development	$ 1,514	$ 2,312
Selling and marketing	1,719	1,013
General and administrative	4,298	5,434
	$ 7,531	$ 8,759

As of December 31, 2020, the Company had an aggregate of $12,103 of unrecognized stock-based compensation cost, which is expected to be recognized over a weighted average period of 2.6 years.

14. 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, 2020 and 2019:

	Year Ended December 31, 2020	2019
Numerator:		
Net loss	$ (155,636)	$ (86,372)
Denominator:		
Weighted average common shares outstanding, basic and diluted	60,752,225	45,273,231
Net loss per share basic and diluted	$ (2.56)	$ (1.91)

The Company excluded the following common stock equivalents, outstanding as of December 31, 2020 and 2019, from the computation of diluted net loss per share attributable to common stockholders for the years ended December 31, 2020 and 2019 because they had an anti-dilutive impact due to the net loss incurred for the periods. The

Company also excluded the shares issuable upon conversion of the 2026 Convertible Notes from the computation of diluted net loss per share for the year ended December 31, 2020 and 2019 because they had an anti-dilutive impact.

	December 31,	
	2020	2019
Options to purchase common stock	9,114,735	7,920,417
Shares issuable upon conversion of 2026 Convertible Notes, if converted	5,769,232	5,769,232
Warrants for the purchase of common stock	18,939	18,939
	14,902,906	13,708,588

15. Commitments and Contingencies

Intellectual Property Licenses

The Company has a license agreement with Incept, LLC ("Incept") to use and develop certain patent rights (the "Incept License"). Under the Incept License, as amended and restated, the Company was granted a worldwide, perpetual, exclusive license 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. Through December 31, 2020, royalties paid under this agreement related to product sales were $575 and have been charged to cost of product revenue.

On September 13, 2018, the Company entered into a second amended and restated license agreement (the "Second Amended Agreement") with Incept. The Second Amended Agreement amends and restates in full the Company's prior amended and restated Incept License (the "Prior Agreement" or "Original License") to expand the scope of the Company's intellectual property license and modify future intellectual property ownership and other rights thereunder.

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners, and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors and senior management team that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnifications. As of December 31, 2020, the Company was not aware of any claims that could have a material effect on its financial position, results of operations or cash flows, and it has not accrued any liabilities related to such obligations in its consolidated financial statements as of December 31, 2020.

Collaboration Agreement

On October 10, 2016, the Company entered into a Collaboration Agreement with Regeneron which the parties amended in May 2020 (Note 8). If the Option to enter into an exclusive worldwide license is exercised, Regeneron will be obligated to conduct further preclinical development and an initial clinical trial under a collaboration plan. The Company is obligated to reimburse Regeneron for certain development costs incurred by Regeneron under the collaboration plan during the period through the completion of the initial clinical trial, subject to a cap of $25,000, which cap may be increased by up to $5,000 under certain circumstances; the timing of such payments are not known. If Regeneron elects to proceed with further development following the completion of the collaboration plan, it will be solely responsible for conducting and funding further development and commercialization of product candidates. If the Option is exercised, Regeneron is required to use commercially reasonable efforts to research, develop and commercialize at least one Licensed Product. Such efforts shall include initiating the dosing phase of a subsequent

clinical trial within specified time periods following the completion of the first-in-human clinical trial or the initiation of preclinical toxicology studies, subject to certain extensions.

16. 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 8 years. Certain leases include one or more options to renew, exercised at the Company's sole discretion, with renewal terms that can extend the lease term from one year to six years. All of the Company's leases qualify as operating leases.

In October 2017, the Company entered into an amendment to a lease agreement for the Company's laboratory and manufacturing space located at 34 Crosby Drive and 36 Crosby Drive, each in Bedford, Massachusetts. The lease term commenced on June 30, 2018 and will expire on July 31, 2023.

In June 2016, the Company entered into a lease agreement 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 for two additional periods of five years by delivering written notice of the exercise not earlier than fifteen months nor later than 12 months before expiration of the original term.

On April 4, 2019, the Company entered into a non-cancelable lease for 30,036 square feet of space located at 24 Crosby Drive in Bedford, Massachusetts to be used for office space. The five-year lease commenced on April 18, 2019 and terminates on March 24, 2024 and does not include any lease renewal options.

	For the Year Ended December 31, 2020	For the Year Ended December 31, 2019
Operating lease costs	$ 2,418	$ 2,070
Variable lease costs	677	538
Total lease costs	$ 3,095	$ 2,608

The following table summarizes the presentation in the Company's consolidated balance sheet of its operating leases:

	Balance sheet location	December 31, 2020	December 31, 2019
Assets:			
Operating lease assets	Operating lease assets	$ 5,844	$ 6,655
Liability:			
Current operating lease liabilities	Operating lease liabilities	$ 1,358	$ 1,126
Non-current operating lease liabilities	Operating lease liabilities, net of current portion	7,548	8,905
Total Operating lease liabilities:		$ 8,906	$ 10,031

The minimum lease payments for the next five years and thereafter are expected to be as follows:

Year Ending December 31,	December 31, 2020
2021	2,483
2022	2,549
2023	2,353
2024	1,569
2025	1,447
Thereafter	2,366
Total lease payments	$ 12,767
Less: interest	3,861
Present value of operating lease liabilities	$ 8,906

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, 2020	December 31, 2019
Weighted average remaining lease term in years	5.6	6.47
Weighted average discount rate	13.55 %	13.55 %

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, 2020	For the Year Ended December 31, 2019
Cash paid for amounts included in the measurement of lease liabilities	$ 2,418	$ 2,215

17. Income Taxes

During the years ended December 31, 2020 and 2019, 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,	
	2020	2019
Federal statutory income tax rate	21.0 %	21.0 %
Research and development tax credits	1.0	2.1
State taxes, net of federal benefit	1.0	2.7
Stock-based compensation	—	(1.3)
Derivative liability	(11.5)	—
Other	—	(0.5)
Change in the valuation allowance	(11.5)	(24.0)
Effective income tax rate	— %	— %

Changes in the valuation of the derivative liability do not provide a future tax benefit. To the extent the deferred tax asset related to the derivative liability exceeds the deferred tax liability related to the 2026 Convertible Notes, the excess is recorded as a permanent item.

Net deferred tax assets consisted of the following:

	December 31,	
	2020	2019
Deferred tax assets:		
Net operating loss carryforwards	$ 90,797	$ 70,317
Tax credit carryforwards	13,514	11,966
Capitalized start-up costs	514	695
Capitalized research and development expenses, net	10,657	14,521
Operating lease liabilities	2,066	2,505
Derivative liability	3,061	3,028
Accrued expenses and other	6,828	6,987
Total deferred tax assets	127,437	110,019
Valuation allowance	(123,020)	(105,062)
Net deferred tax assets	4,417	4,957
Deferred tax liabilities:		
Operating lease right of use assets	(1,356)	(1,662)
2026 Convertible Notes	(3,061)	(3,295)
Total deferred tax liabilities	(4,417)	(4,957)
Net deferred tax assets	$ —	$ —

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2020 and 2019 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,	
	2020	2019
Valuation allowance as of beginning of year	$ 105,062	$ 84,343
Increases recorded to income tax provision	17,958	20,719
Valuation allowance as of end of year	$ 123,020	$ 105,062

As of December 31, 2020, the Company had net operating loss (“NOL”) carryforwards for federal and state income tax purposes of $354,745 and $274,939, 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 $229,113, can be carried forward indefinitely. As of December 31, 2020, the Company also had available research and development tax credit carryforwards for federal and state income tax purposes of $9,226 and $4,988, 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 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, 2020 and 2019.

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2020 or 2019.

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 December 31, 2016 to the present. Earlier years may be examined to the extent that tax credit or net operating loss carryforwards are used in future periods. The Company's policy is to record interest and penalties related to income taxes as part of its income tax provision. As of December 31, 2020 and 2019, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's statements of operations and comprehensive loss.

18. 401(k) Savings Plan

The Company established a defined contribution savings plan under Section 401(k) of the Internal Revenue Code. This 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. Through December 31, 2020, no contributions have been made to the plan by the Company.

19. Related Party Transactions

Since October 2017, the Company has engaged McCarter English LLP ("McCarter") to provide legal services to the Company, including with respect to intellectual property matters. Mr. Jonathan M. Sparks, Ph.D., a partner at McCarter & English, has also served in the capacity as the Company's in-house counsel from October 2017 through August 31, 2020. The Company incurred fees for legal services rendered by McCarter of $766 and $1,119 for the years ended December 31, 2020 and 2019, respectively. As of December 31, 2020 and 2019, there was $47 and $107 recorded in accounts payable for McCarter. As of December 31, 2020 and 2019, there was $0 and $242 recorded in accrued expenses for McCarter.

20. Restructuring and Other Costs

On November 6, 2019, the Board of Directors approved an operational restructuring to eliminate a portion of the Company's workforce to reduce expenses. As part of this operational restructuring, the Company reduced headcount by approximately 22%. The Company completed the restructuring in the fourth quarter of 2019 and recorded total restructuring costs of approximately $554 in total costs and operating expenses in the consolidated statements of operations and comprehensive loss, all of which was paid.

21. Subsequent Events

The number of shares of common stock that may be issued under the 2014 Plan is subject to increase on the first day of each fiscal year, beginning on January 1, 2015 and ending on December 31, 2024, equal to the least of 1,659,218 shares of the Company's common stock, 4% 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, 2021, the number of shares available for issuance under the 2014 Plan increased by 1,659,218.

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, 2021, the number of shares available for issuance under the ESPP increased by 207,402.

On January 29, 2021, warrants covering 18,939 shares were exercised via net share settlement, and the Company issued 11,737 shares of common stock as a result of the exercise.

On February 1, 2021, the Company issued to the Senior Vice President, Clinical Development, a non-statutory stock option to purchase an aggregate of 100,000 shares of its common stock at an exercise price of $18.70 per share subject to a time-based vesting and a non-statutory stock option to purchase 50,000 shares of its common stock at an exercise price of $18.70 per share subject to performance-based vesting. The stock option was issued under the Company's 2019 Inducement Plan as an inducement material to such individual's acceptance of an offer of employment with the Company in accordance with Nasdaq Listing Rule 5635(c)(4). Subject to her continued service to the Company, the time-based stock option will vest over a four-year period, with 25% of the shares underlying the option award vesting on the one-year anniversary of the grant date and the remaining 75% of the shares underlying the award vesting monthly thereafter. The performance-based stock option vests and becomes exercisable in whole or in part if the Company achieves specified milestones, subject to continued service to the Company through the applicable vesting dates. The stock options are subject to the terms and conditions of stock option agreements covering the grant and the Company's 2019 Inducement Plan, as amended to date.

Exhibit 10.9

OCULAR THERAPEUTIX, INC.

Amendment to 2019 Inducement Stock Incentive Plan

Ocular Therapeutix, Inc's 2019 Inducement Stock Incentive Plan (the "**Plan**"), pursuant to Section 11(d) thereof, is hereby amended as set forth below.

The first sentence of Section 4(a) of the Plan be, and hereby is, deleted in its entirety and replaced with the following in lieu thereof:

"Subject to adjustment under Section 9, Awards may be made under the Plan for up to 1,054,000 shares of common stock, $0.0001 par value per share, of the Company (the "Common Stock")."

Adopted by the Board of Directors: December 10, 2020

Exhibit 10.19

Execution Copy

EMPLOYMENT AGREEMENT

This EMPLOYMENT AGREEMENT (the "Agreement") is made on August 28, 2020, by and between Ocular Therapeutix, Inc., a Delaware corporation (the "Company"), and Philip C. Strassburger ("Executive") and the employment relationship between the Company and the Executive shall be governed by this Agreement commencing as of the Effective Date (as defined below) and continuing in effect until terminated by either party in accordance with this Agreement. 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.

(a) Capacity. Executive shall serve the Company as General Counsel, reporting to the Company's Chief Executive Officer (the "CEO"). During the Term (as defined below) of Executive's employment with the Company, Executive shall, subject to the direction of the CEO, have the responsibilities, duties and authority commensurate with the position of General Counsel and shall perform such other duties as may from time to time be assigned to him by the CEO that are consistent with his position as General Counsel. The Company may change Executive's position, duties, and work location as it deems necessary, provided such changes are commensurate with a General Counsel position at similar companies and do not otherwise amount (either singly or in the aggregate) to a "Good Reason" event as defined in Section 3(c).

(b) Devotion of Duties; Representations. During the Term of Executive's employment with the Company, Executive shall devote 100% of his best efforts and full 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 Board of Directors (the "Board")), undertake any other employment from any person or entity or serve as a director of any other company; provided, however, that (i) Executive shall be permitted to provide cooperation and assistance reasonably requested by his prior employer and continue his advisory board membership with Accencio, (ii) the Company will entertain requests as to such other employment or directorships in good faith and (iii) Executive will be eligible to participate in any policy relating to outside activities that is applicable to the senior executives of the Company and approved by the Board after the date hereof, and provided further that in no event may any business 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.

2. Term of Employment.

(a) Executive's employment hereunder shall begin on the first business day following his last day of employment with his prior employer (the "Effective Date"), which is expected to be on or before September 15, 2020 and shall be no later than September 30, 2020.

For the avoidance of doubt, if this Agreement does not become effective by September 30, 2020, it shall be null and void. Executive's employment hereunder shall 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 (i) is unable to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment which can be expected to result in death or can be expected to last for a continuous period of not less than twelve (12) months or (ii) is, by reason of any medically determinable physical or mental impairment which can be expected to last for a continuous period of not less than twelve (12) months, receiving income replacement benefits for a period of not less than three (3) months under an accident and health plan covering employees of the Company. Such incapacity shall be determined by a physician chosen by the Company and reasonably satisfactory to Executive (or Executive's legal representative) upon examination requested by the Company (to which Executive hereby agrees to submit). Notwithstanding the foregoing, such Disability must result in Executive becoming "Disabled" within the meaning of Section 409A(a)(2)(C) of the Internal Revenue Code of 1986, as amended (the "Code") and the guidance issued thereunder. (In this Agreement we refer to Section 409A of the Code and any guidance issued thereunder as "Section 409A.")

(B) For Cause (as defined below); or

(C) Subject to Section 4 hereof, 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; or

(B) By written notice to the Company for Good Reason (as defined below), effective on the date specified in such notice.

The term of Executive's employment by the Company under this Agreement is referred to herein as the "Term."

(b) Definition of "Cause". For purposes of this Agreement, "Cause" shall, pursuant to the reasonable good faith determination by the Company as documented in writing, 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 a material provision of this Agreement, provided that any breach of Executive's obligations with respect to Sections 5 or 6 of this Agreement, subject to the cure provision in the next sentence, shall be deemed "material." In respect of the events described in clauses (i) 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 reasonable discretion. If cured, such events or grounds shall no longer be deemed a basis for a termination of Executive for "Cause," at any time during Executive's employment.

(c) Definition of "Good Reason". For purposes of this Agreement, "Good Reason" shall mean any of the following, unless (i) the basis for such Good Reason is cured within a reasonable period of time (in the light of the cure appropriate to the basis of such Good Reason, but in no event less than thirty (30) nor more than ninety (90) days) 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 to the condition that would otherwise be a basis for Good Reason:

(i) A change in the principal location at which Executive provides services to the Company to a location more than fifty (50) miles from such principal location other than in a direction that reduces Executive's daily commuting distance (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 the corporate headquarters 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 the Effective Date;

(iii) A material reduction in Executive's base salary;

(iv) A material breach by the Company of this Agreement, which breach has not been cured within thirty (30) days after written notice thereof by Executive; or

(v) Failure to obtain the assumption (assignment) of this Agreement by any successor to the Company.

(d) Definition of "Corporate Change". For purposes of this Agreement, "Corporate Change" shall mean any circumstance in which (i) the Company is not the surviving entity in any merger, consolidation or other reorganization (or survives only as a subsidiary or affiliate of an entity other than a previously wholly-owned subsidiary of the Company); (ii) the Company sells, leases or exchanges all or substantially all of its assets to any other person or entity (other than a wholly-owned subsidiary of the Company); (iii) any person or entity, including a "group" as contemplated by Section 13(d)(3) of the Securities Exchange Act of 1934 (excluding, for this purpose, the Company or any subsidiary, or any employee benefit plan of the Company or any subsidiary, or any "group" in which all or substantially all of its members or its members' affiliates are individuals or entities who are or were beneficial owners of the Company's outstanding shares prior to the initial public offering of the Company's common stock), acquires or gains ownership or control (including, without limitations, powers to vote) of more than 50% of the outstanding shares of the Company's voting stock (based upon voting power); or (v) as a result of or in connection with a contested election of directors, the persons who were directors of the Company before such election shall cease to constitute a majority of the Board of Directors of the Company. Notwithstanding the foregoing, a "Corporate Change" shall not occur as a result of a merger, consolidation, reorganization or restructuring after which either (1) a majority of the Board of Directors of the controlling entity consists of persons who were directors of the Company prior to the merger, consolidation, reorganization or restructuring or (2) all or substantially all of the individuals or entities who were the beneficial owners of the Company's outstanding shares immediately prior to such merger, consolidation, reorganization or restructuring beneficially own, directly or indirectly, more than 50% of the then-outstanding shares of common stock and the combined voting power of the then-outstanding securities entitled to vote generally in the election of directors, respectively, of the resulting or acquiring corporation in substantially the same proportions as their ownership of the Company's outstanding shares immediately prior to the merger, consolidation, reorganization or restructuring. Notwithstanding the foregoing, for any payments or benefits hereunder (including pursuant to Section 4(b)(iii) 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).

3. Compensation.

(a) Base Salary. Executive's minimum base salary during the Term shall be at the rate of $425,000 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. The base salary will be subject to adjustment from time to time in the sole discretion of the Company; provided that, the Company covenants that (A) during the first twelve months of Executive's employment, it shall not reduce Executive's base salary and (B) following such twelve month period, it shall not reduce the base salary below the base salary then in effect immediately prior to the reduction unless (i) Executive consents to such reduction, or (ii) the reduction is in connection with a general reduction of not more than 20% in compensation of senior executives of the Company generally that occurs prior to the effective date of any Corporate Change.

(b) Bonus. In addition to the base salary, the Company may pay Executive an annual bonus (the "Bonus") as determined by the Board, solely in its discretion (it being understood that Executive's target annual bonus shall be 40% of Executive's annual base salary in effect for such year but the actual bonus may be higher or lower in any year in the Board's discretion). The Board's decision to issue a Bonus to Executive in any particular year shall have no effect on the absolute discretion of the Board to grant or not to grant a Bonus in subsequent years. Executive must be an active employee of the Company on December 31 of any 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 earned. For the avoidance of doubt, Executive will first be eligible for the Bonus for the 2020 calendar year. Any Bonus would be prorated for the 2020 calendar year.

(c) Stock Option Grant. Subject to approval by the Compensation Committee of the Board or a majority of the Company's Independent Directors (as defined in Nasdaq Listing Rule 5605(a)(2)), and as a material inducement to Executive entering into employment with the Company, the Company will grant to Executive an option to purchase 350,000 shares of the Company's common stock (the "Option"). The Option is subject to adjustment for stock splits, combinations or other recapitalizations. The exercise price per share of the Option shall be equal to the last reported sale price per share of the common stock on the Nasdaq stock exchange on the effective date of grant of the Option. The Option shall be issued outside the Company's 2014 Equity Incentive Plan, as amended, as an "inducement grant" within the meaning of Nasdaq Listing Rule 5635(c)(4), will be a non-qualified stock option for United States tax purposes and will be subject to all of the terms and conditions set forth in a written agreement covering the Option, including, if applicable, the Company's 2019 Inducement Stock Incentive Plan.

(d) Vacation. Executive shall be entitled to take 20 (twenty) days of paid vacation during each year of the Term to be taken at such time or times as shall be mutually convenient and consistent with his 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.

(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 stock option or similar plans relating to the grant of equity securities of the Company. These benefits may be modified or changed from time to time at the sole discretion of the Company. Where a particular benefit is subject to a formal plan (for example, medical or life insurance), eligibility to participate in and receive any particular 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.

(f) Reimbursement of Expenses. Executive shall be entitled to reimbursement for all ordinary and reasonable out-of-pocket business expenses that are

reasonably incurred by him in furtherance of the Company's business in accordance with reasonable policies adopted from time to time by the Company for senior executives, subject to Section 4(d)(v).

(g) Sign on Bonus. The Company will pay Executive a one-time sign on bonus of $100,000 subject to tax deductions and withholdings, which will be paid within thirty (30) days of the Effective Date. If Executive voluntarily terminates his employment without Good Reason or his employment is terminated by the Company for Cause within one year of the Effective Date, Executive will be responsible for reimbursing the Company for the total amount of this bonus within thirty (30) days of the termination of Executive's employment.

(h) Relocation Expenses. In order to assist with Executive's relocation to the Greater Boston area, the Company will reimburse Executive for up to an amount to be reasonably determined by the Company in consultation with the Executive (the "Relocation Amount") for reasonable moving expenses incurred by him in connection with his relocation within one year of the Effective Date. The Relocation Amount will be paid to Executive in a lump sum within sixty (60) days following his relocation to the Greater Boston area, provided that he delivers to the Company reasonable substantiation and documentation of such expenses. For the avoidance of doubt, no part of the Relocation Amount will be paid to Executive prior to his relocation to the Greater Boston area, and no expenses will be reimbursed if incurred after he ceases to be employed by the Company for any reason. Further, if Executive voluntarily terminates his employment without Good Reason or his employment is terminated by the Company for Cause within one year of the Effective Date, Executive will be responsible for reimbursing the Company for the total Reimbursement Amount within thirty (30) days of the termination of his employment.

4. Severance Compensation.

(a) In the event of any termination of Executive's employment for any reason, the Company shall pay Executive (or Executive's estate) such portions of Executive's base salary as have accrued prior to such termination and have not yet been paid, together with (i) amounts for accrued unused vacation days (as provided above), (ii) 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 and (iii) 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 for the year of such termination which would have been earned if such termination had not occurred (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 a Good Reason or (ii) by the Company without Cause, the Company shall pay to Executive the Accrued Obligations. In addition, the Company shall pay to Executive the severance benefits set forth below for twelve (12) months, or for eighteen (18) months if such termination occurs during the twelve (12) month period following a Corporate Change (the "Protected Period"), following Executive's termination of employment (as applicable, the "Severance Period"). The receipt of any severance benefits provided in this Section shall be

dependent upon Executive's execution and, to the extent applicable, non-revocation of a standard separation and general release of claims agreement, substantially in the form attached hereto as Exhibit A (the "Release"), which Release contains, among other things, a release of all releasable claims, non-disparagement and cooperation obligations, and a twelve-month post-employment non-competition provision, which 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 benefits shall be paid or commence, as applicable, on the first payroll period following the date the Release becomes effective (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, then the Payment Date shall be no earlier than January 1 of such subsequent calendar year.

(i) The Company shall continue to pay Executive his base salary for the Severance Period in accordance with the Company's payroll practice, 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 his employment terminates through the Payment Date. Notwithstanding the foregoing, if Executive's termination of employment occurs during the Protected Period, the Company shall pay Executive his base salary for the Severance Period in a lump sum on the Payment Date.

(ii) Only if Executive's employment is terminated (A) by Executive for a Good Reason or (B) by the Company without Cause, in each case during the Protected Period, the Company shall pay Executive an amount equal to one and one-half times his 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.

(iii) Only if Executive's employment is terminated (A) by Executive for a Good Reason or (B) by the Company without Cause, in each case during the Protected Period, one hundred percent (100%) of Executive's outstanding unvested equity awards granted under the Company's equity and long-term incentive plan(s) prior to his termination (including, but not limited to, the Option) shall vest immediately.

(iv) The Company shall continue to provide Executive and his then- enrolled eligible dependents with group health insurance and shall continue to pay the amount of the premium as in effect on the date of such termination for the Severance Period commencing on the effective date of such termination, subject to applicable law and the terms of the respective policies and provided Executive elects and is eligible to continue receiving group health insurance pursuant to COBRA; provided that the Company's obligation to provide the benefits contemplated herein shall terminate upon Executive's 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) In the event that Executive's employment hereunder is terminated (i) by Executive for other than a Good Reason, or (ii) by the Company for Cause, or (iii) as a result of Executive's death or Disability, then the Company will pay to Executive the Accrued

Obligations. The Company shall have no obligation to pay Executive (or Executive's estate) any other compensation following such termination except as provided in Section 4(a).

(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 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 Section 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 him (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:

(1) "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.

(2) "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 determine and 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 he agrees with the Company's determination pursuant to the preceding sentence or (B) that he disagrees with such determination, in which case he 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 he 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 he 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. Employee Covenants.

(a) Confidential Information. Executive recognizes and acknowledges the competitive and proprietary aspects of the business of the Company, and that as a result of Executive's employment, Executive recognizes and acknowledges that he has had and will continue to have access to, and has been and will continue to be involved in the development of, Confidential Information (as defined below) of the Company. As used herein, "Confidential Information" shall mean and include trade secrets, knowledge and other confidential information of the Company, which Executive has acquired, no matter from whom or on what matter such knowledge or information may have been acquired, heretofore or hereafter, concerning the content and details of the business of the Company, and which is not known to the general public, including but not limited to: confidential and proprietary information supplied to Executive with the legend "Confidential and Proprietary," or equivalent, the Company's marketing and customer support strategies, suppliers and customers, marketing and selling, business plans, licenses, the Company's financial information, including sales, costs, profits, prices, pricing methods, budgets and unpublished financial statements, the Company's internal organization, employee information obtained pursuant to Executive's duties and responsibilities, information regarding the skills and compensation of other employees of the Company obtained pursuant to Executive's duties and responsibilities and customer lists, the Company's technology, including products, discoveries, inventions, research, experimental and development efforts, clinical studies, processes, hardware/software design and maintenance tools, samples, media and/or molecular structures (and procedures and formulations for producing any such samples, media and/or molecular structures), formulas, methods, know-how and show-how, designs, prototypes, plans for research and new products, and all derivatives, improvements and enhancements of any of the above and information of third parties as to which the Company has an obligation of confidentiality.

(i) For as long as Executive is employed and at all times thereafter, Executive shall not, directly or indirectly, communicate, disclose or divulge to any person or entity, or use for Executive's own benefit or the benefit of any person (other than the Company), any Confidential Information, except as permitted in subparagraph (iii) below. Upon termination of Executive's employment, or at any other time at the request of the Company, Executive agrees to deliver promptly to the Company all Confidential Information, including, but not limited to, customer and supplier lists, files and records, in Executive's possession or under Executive's control. Executive further agrees that he will not make or retain any copies of any of the foregoing and will so represent to the Company upon termination of Executive's employment. However, nothing in this Agreement or elsewhere shall prohibit Executive from retaining, and using appropriately, copies of documents relating to Executive's personal rights and obligations, or from making disclosures, in confidence, to his attorney and financial advisor for the purpose of obtaining professional advice.

(ii) Executive shall disclose immediately to the Company any trade secrets or other Confidential Information conceived or developed by Executive at any time during Executive's employment. Executive hereby assigns and agrees to assign to the Company Executive's entire right, title and interest in and to all Confidential Information. Such assignment shall include, without limitation, the rights to obtain

patent or copyright protection thereon in the United States and foreign countries. Executive agrees to provide all reasonable assistance to enable the Company to prepare and prosecute any application before any governmental agency for patent or copyright protection or any similar application with respect to any Confidential Information. Executive further agrees to execute all documents and assignments and to make all oaths necessary to vest ownership of such intellectual property rights in the Company, as the Company may reasonably request. These obligations shall apply whether or not the subject thereof was conceived or developed at the suggestion of the Company, and whether or not developed during regular hours of work or while on the premises of the Company.

(iii) Except as set forth below, Executive shall at all times, both during and after termination of this Agreement by either Executive or the Company, maintain in confidence and shall not, without prior written consent of the Company, use, except in the course of performance of Executive's duties for the Company or as required by legal process (provided that Executive will promptly notify the Company of such legal process except with respect to any confidential government investigation), disclose or give to others any Confidential Information. In the event Executive is questioned by anyone not employed by the Company or by an employee of or a consultant to the Company not authorized to receive such information, in regard to any such information or any other secret or confidential work of the Company, or concerning any fact or circumstance relating thereto, Executive will promptly notify the Company. Notwithstanding the foregoing, however, nothing in this Agreement or elsewhere prohibits Executive from 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. Executive is not required to notify the Company of any such communications; provided, however, that nothing herein authorizes the disclosure of information Executive obtained through a communication that was subject to the attorney-client privilege. Further, notwithstanding Executive's confidentiality and nondisclosure obligations, Executive is 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."

(b) Non-Competition and Non-Solicitation. Executive recognizes that the Company is engaged in a competitive business and that the Company has a legitimate interest in protecting its trade secrets, confidential business information, and customer, business development partner, licensee, supplier, and credit and/or financial relationships. Accordingly, in exchange for valuable consideration, including without limitation Executive's access to

confidential business information, employment by the Company, and, with respect to the non-competition restrictions, the Option granted as described in Section 3(c) which Executive hereby explicitly acknowledges and agrees has been mutually agreed upon by Executive and the Company, is fair and reasonable, and is sufficient consideration in exchange for the non-competition restriction, Executive agrees as follows:

(i) Non-Competition. During the Restricted Period (as defined below), Executive will not, in the Applicable Territory (as defined below), directly or indirectly, whether for himself or for any other person or entity, and whether as a proprietor, principal, shareholder, partner, agent, employee, consultant, independent contractor, or in any other capacity whatsoever, undertake or have any interest in (other than the passive ownership of publicly registered securities representing an ownership interest of less than 1%), or engage or assist others in engaging in, any business or enterprise that is competitive with the Company's business, 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 any product or service researched, developed, manufactured, marketed, licensed, sold or provided, or planned to be researched, developed, manufactured, marketed, licensed, sold or provided by the Company or any of its affiliates or subsidiaries (a "Competitive Business"), if Executive would be performing job duties or services for the Competitive Business that are of a similar type that Executive performed for the Company at any time during the last two (2) years of Executive's employment. As a senior leader for the Company, Executive acknowledges and agrees that, in the performance of Executive's duties for the Company (including, without limitation, assisting the Company with its overall business strategy), Executive will be privy to and rely upon Confidential Information regarding all aspects of the Company's business and operations. Accordingly, Executive acknowledges and agrees that undertaking a role in a Competitive Business would constitute performing job duties or services of a similar type that Executive performed for the Company. Notwithstanding the foregoing, both Executive and the Company recognize and acknowledge that nothing in this Section 5(b)(i), any other section of this Agreement or elsewhere is intended to or shall be interpreted to (x) restrict Executive's ability, after he ceases to be an employee of the Company, to practice law, in violation of the Massachusetts Rules of Professional Conduct 5.6 or other applicable rules of professional conduct; or (y) expand the scope of Executive's duty to maintain privileged or confidential information obtained in connection with his role as counsel for the Company beyond what is permitted under Massachusetts Rules of Professional Conduct 1.6 and 1.9, or other applicable rules of professional conduct.

(1) Certain Definitions. Solely for purposes of this Section 5(b)(i):

(A) the "Restricted Period" shall include the duration of Executive's employment with the Company and the twelve (12) month period thereafter; provided, however, that the Restricted Period shall automatically be extended to two (2) years following the cessation of Executive's employment if Executive breaches a fiduciary duty to the Company or unlawfully takes, physically or electronically, any property belonging to the Company. Notwithstanding the foregoing, the Restricted Period shall end immediately upon Executive's last day of employment with the Company if : (x) the Company terminates Executive's

employment other than for Cause (as defined in Section 2(b)), or (y) the Company notifies Executive in writing that it is waiving the post-employment restrictions set forth in this Section 5(b)(i) (such notice to be provided no later than Executive's last day of employment or by the seventh (7th) business day following Executive's notice of resignation, if later).

(B) "Applicable Territory" shall mean the geographic areas in which Executive provided services or had a material presence or influence at any time during Executive's last two (2) years of employment. As a senior leader for the Company, Executive acknowledges that Executive's duties and responsibilities require Executive to have a material presence and/or influence anywhere that the Company does business.

(ii) Non-Solicitation. While Executive is employed by the Company and for a period of twelve (12) months after the termination or cessation of such employment for any reason, except in the performance of his duties for the Company, Executive will not directly or indirectly:

(1) initiate contact with (including without limitation phone calls, press releases and the sending or delivering of announcements), or in any manner solicit, directly or indirectly, any customers, business development partners, licensors, licensees, or creditors (including institutional lenders, bonding companies and trade creditors) of the Company in an attempt to induce or motivate them either to discontinue or modify their then prevailing or future relationship with the Company or to transfer any of their business with the Company to any person or entity other than the Company; or

(2) initiate contact with, or in any manner solicit, directly or indirectly, any supplier of goods, services or materials to the Company in an attempt to induce or motivate them either to discontinue or modify their then prevailing or future relationship with the Company or to supply the same or similar inventory, goods, services or materials (except generally available inventory, goods, services or materials) to any person or entity other than the Company; or

(3) directly or indirectly recruit, solicit or otherwise induce or influence any employee or independent contractor of the Company to discontinue or modify his or her employment or engagement with the Company, or employ or contract with any such employee or contractor for the provision of services.

If Executive violates the provisions of any of the preceding paragraphs of this Section 5(b)(ii), Executive shall continue to be bound by the restrictions set forth in such paragraph until a period of twelve (12) months has expired without any violation of such provisions. Further, the twelve (12) month post-employment restrictions set forth in this Section 5(b)(ii) shall be extended to two (2) years if Executive breaches a fiduciary duty to the Company or unlawfully takes, physically or electronically, any property belonging to the Company.

(c) Definition of "Customer". The term "customer" or "customers" shall include any person or entity (a) that is a current customer of the Company, (b) that was a

customer of the Company at any time during the preceding twenty-four (24) months or (c) to Executive's knowledge, to which the Company made a written presentation for the solicitation of business at any time during the preceding twenty-four (24) months.

(d) Reasonableness of Restrictions. Executive further recognizes and acknowledges that (i) the types of employment which are prohibited by this Section 5 are narrow and reasonable in relation to the skills which represent Executive's principal salable asset both to the Company and to Executive's other prospective employers, and (ii) the broad geographical scope of the provisions of this Section 5 is reasonable, legitimate and fair to Executive in light of the global nature of the Company's business, and in light of the limited restrictions on the type of employment prohibited herein compared to the types of employment for which Executive is qualified to earn Executive's livelihood.

(e) Remedies. Executive acknowledges that a breach of this Section 5 will cause great and irreparable injury and damage, which cannot be reasonably or adequately compensated by money damages. Accordingly, Executive acknowledges that the remedies of injunction and specific performance shall be available in the event of such a breach, in addition to money damages, costs and attorneys' fees, and other legal or equitable remedies, and that the Company shall be entitled as a matter of course to an injunction pending trial, without the posting of bond or other security. Any period of restriction set forth in this Section 5 shall be extended for a period of time equal to the duration of any breach or violation hereof.

(f) Notification. Any person employing Executive or evidencing any intention to employ Executive may be notified as to the existence and provisions of this Agreement.

(g) Modification of Covenants; Enforceability. In the event that any provision of this Section 5 is held to be in any respect an unreasonable restriction, then the court so holding may modify the terms thereof, including the period of time during which it operates or the geographic area to which it applies, or effect any other change to the extent necessary to render this section enforceable, it being acknowledged by the parties that the representations and covenants set forth herein are of the essence of this Agreement.

(h) Subsidiaries. For purposes of Sections 5 and 6 of this Agreement, "Company" shall include all direct and indirect subsidiaries of the Company. An entity shall be deemed to be a subsidiary of the Company if the Company directly or indirectly owns or controls 50% or more of the equity interest in such entity.

(i) Acknowledgements. Executive acknowledges that he has the right to consult with counsel prior to signing this Agreement. Executive further acknowledges that he was provided this Agreement by the earlier of the date of (x) a formal offer of employment, and (y) ten (10) business days prior to Executive's commencement of employment with the Company.

6. Ownership of Ideas, Copyrights and Patents.

(a) Property of the Company. Executive agrees that all ideas, inventions, original works of authorship, developments, concepts, know-how, improvements or trade secrets,

whether patentable, copyrightable or not, which Executive may conceive, reduce to practice or develop, alone or in conjunction with another, or others, whether during or out of regular business hours, and whether at the request or upon the suggestion of the Company, or otherwise, in the course of performing services for the Company in any capacity, whether heretofore or hereafter, (collectively, "the Inventions") are and shall be the sole and exclusive property of the Company, and that Executive shall not publish any of the Inventions without the prior written consent of the Company. Executive hereby assigns to the Company all of Executive's right, title and interest in and to all of the foregoing. Executive further represents and agrees that to the best of Executive's knowledge and belief none of the Inventions will violate or infringe upon any right, patent, copyright, trademark or right of privacy, or constitute libel or slander against or violate any other rights of any person, firm or corporation and that Executive will use his best efforts to prevent any such violation.

(b) Cooperation. At any time during or after the Term, Executive agrees that he will fully cooperate with the Company, its attorneys and agents in the preparation and filing of all papers and other documents as may be required to perfect the Company's rights in and to any of such Inventions, including, but not limited to, executing any lawful document (including, but not limited to, applications, assignments, oaths, declarations and affidavits) and joining in any proceeding to obtain letters patent, copyrights, trademarks or other legal rights of the United States and of any and all other countries on such Inventions, provided that any patent or other legal right so issued to Executive, personally, shall be assigned by Executive to the Company without charge by Executive. Executive further designates the Company as his agent for, and grants to the Company a power of attorney with full power of substitution, which power of attorney shall be deemed coupled with an interest, for the purpose of effecting the foregoing assignments from Executive to the Company. Company will bear the reasonable expenses which are incurred by Executive in assisting and cooperating hereunder. Executive waives all claims to moral rights in any Inventions.

7. Disclosure to Future Employers. The Company may provide in its discretion, a copy of the covenants contained in Sections 5 and 6 of this Agreement to any business or enterprise which Executive may directly, or indirectly, own, manage, operate, finance, join, control or in which Executive participates in the ownership, management, operation, financing, or control, or with which Executive may be connected as an officer, director, employee, partner, principal, agent, representative, consultant or otherwise.

8. 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.

9. Insurance. The Company, in its sole discretion, may apply for and procure in its own name (whether or not for its own benefit) policies of insurance insuring Executive's life. Executive agrees to submit to reasonable medical or other examinations and to execute and deliver any applications or other instruments in writing that are reasonably necessary to effectuate such insurance. No adverse employment actions may be based upon the results of any such exam or the failure by the Company to obtain such insurance.

10. No Conflicting Agreements. Executive hereby represents and warrants that Executive has no commitments or obligations inconsistent with this Agreement.

11. Conditions to Employment. Notwithstanding anything to the contrary contained herein, this Agreement and Executive's employment hereunder is subject to and conditioned on satisfactory background and reference checks, and Executive's provision of proof of his right to work in the United States. The Company shall notify Executive by August 31, 2020 if any such background or reference checks have not been completed to its satisfaction.

12. 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: Antony Mattessich Telephone: (781) 357-4000
With an email copy to:	AMattessich@ocutx.com
If to Executive:	Philip Strassburger [last known address on file with the Company]
	With an email copy to: philip.strassburger@gmail.com

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 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 that expressly references the provision of this Agreement being modified or amended.

(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 referencing the terms and provisions being waived and executed by the party entitled to the benefits of such terms or provisions. 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. 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 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 Massachusetts, 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 Massachusetts or of the United States of America for the District of Massachusetts and in Suffolk County in the event of any legal action or proceeding related to the non-competition provision contained in Section 5. 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 12(a) hereof. THE PARTIES IRREVOCABLY WAIVE ANY RIGHT TO TRIAL BY JURY AS TO ALL CLAIMS HEREUNDER.

(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 agrees 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. The provisions of the following Sections of this Agreement are in addition to, and do not limit, each other: Sections 6 and 5(a); Sections 7 and 5(g); Sections 12(k) and 5(f); and Sections 12(l) and 12(d).

(k) Injunctive Relief. Executive hereby expressly acknowledges that any breach or threatened breach of any of the terms and/or conditions set forth in Section 5 or 6 of this Agreement will result in substantial, continuing and irreparable injury to the Company. Therefore, Executive hereby agrees that, in addition to any other remedy that may be available to the Company, the Company shall be entitled to injunctive or other equitable relief by a court of appropriate jurisdiction.

(l) 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.

(m) 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. Delivery of executed counterparts in electronic form (including by portable document format) shall be sufficient for all purposes.

(n) Survival. The provisions of Sections 4, 5, 6, 7, 8, and 12 shall survive the termination of this Agreement and Executive's employment hereunder in accordance with their terms.

[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/ Philip C. Strassburger
Name: Philip C. Strassburger

EXHIBIT A[1]

Sample Separation and Release Agreement

[Insert Date]

[Insert Name]

Dear **[Insert Name]**:

In connection with the termination of your employment with Ocular Therapeutix, Inc. (the "Company") on **[Separation Date]**, you are eligible to receive the Severance Compensation as described in Section 4 (b) of the Employment Agreement executed between you and the Company dated August 28, 2020 (the "Employment Agreement") if you sign and return this letter agreement to me by **[Return Date - 7/21/45 days from date of receipt of this letter agreement] [and it becomes binding between you and the Company**]. By signing and returning this letter agreement [**and not revoking your acceptance]**, you 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 [**seven/twenty-one (21)/forty-five (45)]** [2]days to do so. [**If you sign this letter agreement, you may change your mind and revoke your agreement during the seven (7) day period after you have signed it 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 seven (7) day period.]**

Although your receipt of the Severance Compensation 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.

- You will receive payment for your final wages and any unused vacation time accrued through the Separation Date and you will receive any other "Accrued Obligations" described in Section 4(a) of the Employment Agreement.

- You may, if eligible and at your own cost, elect to continue receiving group medical insurance pursuant to applicable "COBRA" law. Please consult the COBRA materials to be provided under separate cover for details regarding these benefits.

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1 Note: The Company may revise this release agreement in its reasonable discretion to reflect changes in law, additional statutes or claims, benefits, or employee's circumstances, so that the Company receives the benefit of the most complete release of claims that is legally permissible (without releasing employee's right to receive the Severance Compensation and without imposing additional post-employment restrictions), and the Company may also change the timing, if required by applicable law to obtain such release. 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 Consideration period depends upon circumstances of separation.

- 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 9 below. Further, you remain subject to any and all continuing confidentiality, non-competition and/or non-solicitation obligations that you may have pursuant to any previous agreement with the Company, including, as may be applicable and without limitation, the Employment Agreement.

- You must return to the Company no later than the Separation Date all Company property.

The following numbered paragraphs set forth the terms and conditions that will also apply if you timely sign and return this letter agreement **[and do not revoke it in writing within the seven (7) day period]**.

1. **Severance Compensation** - If you timely sign and return this letter agreement [and do not revoke your acceptance], and provided you comply with all of your obligations set forth herein, the Company will provide you with the severance compensation and benefits set forth in Section 4(b) of the Employment Agreement (the "Severance Compensation"), subject to and in accordance with the terms and conditions thereof.

2. **Release** - In consideration of the Severance Compensation, 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, managers, employees, agents, representatives, plan administrators, attorneys, insurers and fiduciaries (each in their individual and corporate capacities) (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, 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 Wage Act, Mass. Gen. Laws ch. 149, § 148 et seq. (Massachusetts law regarding payment of wages and overtime), the Massachusetts Civil Rights Act, Mass. Gen. Laws ch. 12, §§ 11H and 11I, the Massachusetts Equal Rights Act, Mass. Gen. Laws. ch. 93, § 102 and Mass.

Gen. Laws ch. 214, § 1C, 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 Maternity Leave Act, Mass. Gen. Laws ch. 149, § 105D, and the Massachusetts Small Necessities Leave Act, Mass. Gen. Laws ch. 149, § 52D, all as amended; [Insert any other applicable Federal and state citations at the time of termination;] 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 relating to the Employment Agreement); all claims to any 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 nothing in this letter agreement: (i) prevents 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) deprives you of any accrued benefits to which you have acquired a vested right under any employee benefit plan or policy, stock plan or deferred compensation arrangement, any health care continuation to the extent required by applicable law or any agreement, or any right to severance benefits or any other benefits due to you upon termination of employment or thereafter that are described in Section 4 of the Employment Agreement; or (iii) deprives you of any rights you may have to be indemnified by the Company as provided in the Employment Agreement, any other agreement between the Company and you, or pursuant to the Company's Certificate of Incorporation or by-laws. This Release shall not extend to any claims you may have against any persons that are Released Parties to the extent such claims are (i) related solely to your ownership of the Company's stock and (ii) unrelated to your employment with the Company.

3. **Continuing Obligations** - You acknowledge and reaffirm your confidentiality, non-competition and non-disclosure obligations discussed above, as well as any and all confidentiality and/or non-solicitation obligations set forth in any previous agreement you may have with the Company (including without limitation the Employment Agreement), which survive your separation from employment with the Company. In addition, as an express condition of your receipt of the Severance Compensation, you agree that, for a period of twelve (12) months following the Separation Date, you will not, without the prior consent of the Company, directly or indirectly, as a partner, stockholder, director, consultant, joint venture, investor, employee or in any other capacity, work for, provide services, engage in or own, manage, operate or control, or participate in the ownership, management, operation or control of any business or entity that engages in a substantially similar business or line of businesses as those conducted by the Company or any of its direct or indirect subsidiaries for which you worked or served at the time of your separation, in any market where such businesses or entity actually and directly competes against the Company; provided, however, that nothing herein shall prohibit you from owning not more than 1% of any class of securities of a publicly traded entity in any business or entity; and further provided however, that both you and the Company recognize and acknowledge that nothing in this paragraph 3 or elsewhere is intended to or shall

be interpreted to (x) restrict your ability, after you cease to be an employee of the Company, to practice law, in violation of the Massachusetts Rules of Professional Conduct 5.6 or other applicable rules of professional conduct; or (y) expand the scope of your duty to maintain privileged or confidential information obtained in connection with your role as counsel for the Company beyond what is permitted under Massachusetts Rules of Professional Conduct 1.6 and 1.9, or other applicable rules of professional conduct. If any restriction set forth in the foregoing sentence 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 of 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 the restrictions set forth in such paragraph until a period of one year has expired without any violation of such provisions.

4. **Non-Disparagement** - You understand and agree that, to the extent permitted by law and except as otherwise permitted by paragraph 9 below, you will not, 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 Company's business affairs, business prospects, or financial condition. The Company agrees to instruct its officers and members of the leadership team to not, 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, or potential employer, about you.

5. **Cooperation** - You agree that, to the extent permitted by law and upon reasonable request, you shall cooperate fully 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. Your full cooperation in connection with such claims or actions shall include, but not be limited to, being 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. The Company will reimburse you for the reasonable and documented out-of-pocket expenses you may incur in connection with your cooperation under this paragraph 5. You further agree that, to the extent permitted by law or unless you are directed otherwise by a court or government agency, 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.

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 and printers, flash drives and storage devices, wireless handheld devices, cellular phones, tablets, etc.), Company identification, and any other Company-owned property in your possession or control and have left intact all electronic Company documents, including but not limited to those that you developed or helped to develop during your employment, and you have not retained any 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.

7. **Business Expenses and Final Compensation** - You acknowledge that you have been reimbursed by the Company for all business expenses incurred in conjunction with the performance of your employment and that no other reimbursements are owed to you. You further acknowledge that 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 is owed to you except as provided herein.

8. **Confidentiality** - You understand and agree that, to the extent permitted by law and except as otherwise permitted by paragraph 9 below, the terms and contents of this letter agreement, and the contents of the negotiations and discussions resulting in this letter agreement, shall be maintained as confidential by you and your agents and representatives and shall not be disclosed except as otherwise agreed to in writing by the Company.

9. **Scope of Disclosure Restrictions -** Nothing in this letter agreement or elsewhere prohibits you from: (i) communicating with government agencies about possible violations of federal, state, or local laws or otherwise providing information to government agencies: (ii) filing a complaint with government agencies, or participating in government agency investigations or proceedings; (iii) disclosing information required by applicable law, or in confidence to your attorney or professional advisor for the purpose of obtaining professional advice; or (iv) enforcing your rights against the Company. 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."

10. **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 the Company 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 the Company 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.

11. **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.

12. **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.

13. **Acknowledgments** - You acknowledge that you have been given at least [seven (7) / twenty-one (21) / forty-five (45)] days to consider this letter agreement, and that the Company advised 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) 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) 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 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.]**

14. **[Eligibility for Severance Program - 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 title and ages of all individuals eligible or selected for such severance benefit program, and the 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.]**

15. **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 state and represent that you have had an opportunity to fully discuss and review the terms of this letter agreement with an attorney. 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. Further, you acknowledge that the restrictions referenced and contained in paragraphs 3 and 4 of this letter agreement are 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 is likely to 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 which may be available, shall have the right to obtain an injunction from a court restraining such a breach or threatened breach without posting a bond and the right to specific performance of such provisions and you and hereby waive the adequacy of a remedy at law as a defense to such relief.

16. **Applicable Law** - 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. You 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.

17. **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. Notwithstanding the foregoing, if there is a conflict between the non-competition obligations set forth in paragraph 3 herein and the noncompetition obligations set forth in Section 5(b)(i) of the Employment Agreement, such conflict will be resolved in the manner most protective of the Company.

18. **Tax Acknowledgement** - In connection with the Severance Compensation, 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 Compensation 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 the Severance Compensation.

[Remainder of Page Intentionally Left Blank]

If you have any questions about the matters covered in this letter agreement, please call me.

Very truly yours,

By: _____
[Name]
[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 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) days.]**

_____ _____
[Insert 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.[3]

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[3] Note: All footnotes will be removed from the final execution version of this agreement.

Exhibit 10.36

SUPPLEMENT

This Supplement (this "Supplement") to License Agreement by and between Ocular Therapeutix, Inc. and Affamed Therapeutics Limited is made and entered into as of January 18, 2021.

WHEREAS, Ocular Therapeutix, Inc. ("Ocular") and Affamed Therapeutics Limited ("Affamed") entered into a License Agreement dated as of October 28, 2020 (the "License Agreement"); and

WHEREAS, Ocular and Affamed desire to supplement the License Agreement by adding a reference to two patents to Exhibit A to the License Agreement;

NOW THEREFORE, the Parties agree as follows:

1. All terms used in this Supplement and not defined shall have the meanings ascribed to them in the License Agreement.

2. Exhibit A is supplemented by adding the following:

- KR20190057353A
- CN102395401B

3. Except as supplemented hereby, each of the terms and provisions of the License Agreement shall remain in full force and effect.

4. This Supplement may be executed in counterparts, all of which taken together shall be regarded as one and the same instrument.

IN WITNESS WHEROF, the Parties have executed this Supplement through their duly authorized representatives to be effective as of the Effective Date.

OCULAR THERAPEUTIX, INC.

By: /s/ Antony Mattessich
Name: Antony Mattessich
Title: President and Chief Executive Officer

AFFAMED THERAPEUTICS LIMITED

By: /s/ Dayao Zhao
Name: Dayao Zhao
Title: CEO

Exhibit 21.1

Subsidiaries of Ocular Therapeutix, Inc.

	Jurisdiction of Incorporation or Organization
Ocular Therapeutix Europe B.V.	The Netherlands

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. 333-229085 333-230659 and 333-251327) and Form S-8 (Nos. 333-198240, 333-202886, 333-210059, 333-216622, 333-223513, 333-230126 and 333-237115) of Ocular Therapeutix, Inc. of our report dated March 11, 2021 relating to the financial statements, which appears in this Form 10-K.

/s/PricewaterhouseCoopers LLP
Boston, Massachusetts
March 11, 2021

Exhibit 31.1

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, 2021

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, 2021

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, 2020 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, 2021

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, 2020 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, 2021

By: /s/ Donald Notman
Donald Notman
Chief Financial Officer
(Principal Financial and Accounting Officer)