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

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**FORM 10-K**

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(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, 2018

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

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**Ocular Therapeutix, Inc.**

(Exact name of registrant as specified in its charter)

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Delaware  
(State or other jurisdiction of  
incorporation or organization)

15 Crosby Drive  
Bedford, MA  
(Address of principal executive offices)

20- 5560161  
(I.R.S. Employer  
Identification No.)

01730  
(Zip Code)

(781) 357-4000

(Registrant's telephone number, including area code)  
Securities registered pursuant to Section 12(b) of the Act:

Title of each class  
Common Stock, \$0.0001 par value per share

Name of each exchange on which registered  
Nasdaq Global Market

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

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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 if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

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	<input type="checkbox"/>	Accelerated filer	<input checked="" type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
	<input type="checkbox"/>	Emerging growth company	<input checked="" type="checkbox"/>

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

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

As of June 29, 2018, the aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant was approximately \$224 million. The number of shares outstanding of the registrant's class of common stock, as of March 1, 2019: 42,836,572

**DOCUMENTS INCORPORATED BY REFERENCE**

Part III of this Annual Report incorporates by reference information from the definitive Proxy Statement for the registrant's 2019 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, 2018.

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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 plans to develop and commercialize DEXTENZA<sup>®</sup> and our product candidates based on our proprietary bioresorbable hydrogel technology platform;
- our ability to manufacture DEXTENZA in compliance with current Good Manufacturing Practices, or cGMP;
- our ability to build and 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 and OTX-TP and our other product candidates;
- our plans to raise additional capital, including through equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements, royalty agreements and marketing and distribution arrangements;
- our ongoing and planned clinical trials, including our Phase 3 clinical trials of OTX-TP for the treatment of glaucoma and ocular hypertension, our Phase 1 clinical trial of OTX-TIC for the reduction of intraocular pressure in patients with glaucoma and ocular hypertension and our Phase 1 clinical trial of OTX-TKI for the treatment of wet age-related macular degeneration, or wet AMD;
- our ability to resolve the U.S. Food and Drug Administration warning letter received with respect to ReSure<sup>®</sup> Sealant on October 18, 2018;
- 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 reimbursement for our products;
- our estimates regarding the potential market opportunity for DEXTENZA, ReSure Sealant, OTX-TP, and our other product candidates;
- the preclinical development of our intravitreal depot with protein-based or small molecule drugs, including tyrosine kinase inhibitors, for the treatment of wet AMD, and other retinal diseases;
- 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, and other serious retinal diseases;

- our capabilities and strategy related to, 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;
- 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 needs for additional financing;
- the impact of government laws and regulations;
- the costs and outcomes of legal actions and proceedings, including any investigations by the Securities and Exchange Commission, and any intellectual property proceedings;
- our ability to continue as a going concern; 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 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.

## 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 of varying duration in our product candidates.

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.

We currently incorporate therapeutic agents that have previously received regulatory approval, including small molecules and proteins, into our hydrogel technology with the goal of providing local programmed-released delivery of drug to the eye. We believe that our local programmed-release 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 intracanalicular inserts, intracameral implants and intravitreal implants. We have products and product candidates in clinical and preclinical development applying this technology to treat post-surgical ocular pain and inflammation, allergic conjunctivitis, dry eye disease, glaucoma and ocular hypertension, and wet age-related macular degeneration, or wet AMD, among other conditions.

On December 3, 2018, we announced that the FDA approved our new drug application, or NDA, for DEXTENZA<sup>®</sup> (dexamethasone ophthalmic insert) 0.4mg for intracanalicular use for the treatment of ocular pain following ophthalmic surgery. DEXTENZA is the first FDA-approved intracanalicular insert delivering dexamethasone to treat post-surgical ocular pain for up to 30 days with a single administration. We are also evaluating DEXTENZA for the treatment of post-surgical ocular inflammation and allergic conjunctivitis.

We are developing our product candidate OTX-TP (intracanalicular travoprost insert) for the reduction of intraocular pressure, or IOP, in patients with glaucoma and ocular hypertension. Both DEXTENZA and OTX-TP are local programmed-release, drug-eluting, preservative-free intracanalicular inserts that are placed into the canaliculus through a natural opening called the punctum located in the portion of the lower eyelid near the nose.

Our earlier stage assets include two development programs that have initiated clinical trials: OTX-TIC, an intracameral travoprost implant for the reduction of IOP in patients with glaucoma and ocular hypertension when greater IOP reduction is needed, and OTX-TKI, an intravitreal injection by fine gauge needle of a hydrogel, anti-angiogenic formulation of a tyrosine kinase inhibitor, or TKI, for the treatment of wet AMD. We also 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 VEGF inhibitor, aflibercept, currently marketed under the brand name Eylea.

In addition to our ongoing drug product development, we currently market ReSure<sup>®</sup> Sealant, a hydrogel ophthalmic wound sealant approved by the FDA to seal corneal incisions following cataract surgery. ReSure Sealant is the first and only surgical sealant to be approved by the FDA for ophthalmic use.

Poor patient compliance with eye drop regimens and the need for frequent administration of eye drops at high drug concentrations due to rapid washout by the tears can create challenges in the successful management of ocular diseases and conditions. For example, poor patient compliance can lead to diminished efficacy and disease progression and high drug concentrations can create side effects. We are developing therapies to replace standard of care eye drop regimens with our innovative local programmed-release, drug-eluting intracanalicular inserts. The goal for our intracanalicular insert product candidates is to replace the management of many front-of-the-eye diseases and conditions using frequent,

pulsed eye drop therapy, characterized by significant variations in drug concentration over time, with longer term, extended delivery of therapeutic agents to improve patient outcomes.

In addition to our focus on formulating, developing and commercializing innovative therapies for diseases and conditions of the eye, we are also assessing the potential use of our hydrogel platform technology in other areas of the body.

***DEXTENZA® (dexamethasone ophthalmic insert)***

DEXTENZA incorporates the FDA-approved corticosteroid dexamethasone as an active pharmaceutical ingredient into a hydrogel, drug-eluting intracanalicular insert. In November 2018, the FDA approved our NDA for DEXTENZA for the treatment of post-surgical ocular pain. In connection with our commercial launch of DEXTENZA, we intend to build our own highly targeted, key account sales force that would focus on the ambulatory surgical centers responsible for the largest volumes of cataract surgery. Following our receipt of FDA approval, we submitted on November 30, 2018 an application for a C-code for transitional pass-through payment status and also submitted on December 28, 2018 an application for a J-code for permanent payment status.

A C-code is a unique temporary pricing code established by the Center for Medicare & Medicaid Services (CMS), for the Prospective Payment System and is only valid for claims for hospital outpatient department services and procedures. A J-Code is a permanent code used to report drugs that ordinarily cannot be self-administered.

We have completed three Phase 3 clinical trials of DEXTENZA for the treatment of post-surgical ocular pain and inflammation. The data from two of these three completed Phase 3 clinical trials and a prior Phase 2 clinical trial were used to support our NDA for post-surgical ocular pain. We submitted an NDA supplement, or sNDA, for DEXTENZA for the treatment of post-surgical ocular inflammation in January 2019 and expect the FDA to complete its review of this submission in the second half of 2019.

We have completed two Phase 3 clinical trials of DEXTENZA for the treatment of allergic conjunctivitis. In October 2015, we announced topline results of our first Phase 3 clinical trial for allergic conjunctivitis, and in June 2016 we announced topline results of our second Phase 3 clinical trial for this indication. We expect to initiate a third Phase 3 trial of DEXTENZA for the treatment of allergic conjunctivitis in the second half of 2019. We have also completed a Phase 2 clinical trial of DEXTENZA for the treatment of dry eye disease.

***OTX-TP (intracanalicular travoprost insert)***

Our product candidate OTX-TP incorporates the active pharmaceutical ingredient travoprost, an FDA-approved prostaglandin analog that reduces elevated IOP, into a hydrogel, drug-eluting intracanalicular insert. This preservative-free insert is designed to elute drug for up to 90 days. OTX-TP is being developed as a treatment to lower IOP in patients with primary open angle glaucoma and ocular hypertension. We reported topline results from a Phase 2b clinical trial for this indication in October 2015. We completed an End-of-Phase 2 review with the FDA in April 2016 and initiated the first of two planned Phase 3 clinical trials of OTX-TP in September 2016. Our first Phase 3 trial has completed the target enrollment of 550 patients at approximately 50 sites in the United States. Based on discussions with the FDA, the first Phase 3 clinical trial design includes an OTX-TP treatment arm and a placebo-controlled comparator arm that uses a non-drug eluting hydrogel intracanalicular insert. The primary efficacy endpoint is superiority in the reduction of IOP from baseline in the OTX-TP treatment arm compared to the placebo arm at three diurnal time points at each of three measurement dates, 2, 6 and 12 weeks. We expect that the FDA will require that OTX-TP show both a statistically superior reduction of IOP compared to the placebo and a clinically meaningful reduction of IOP prior to granting marketing approval. We expect topline efficacy data from the first Phase 3 clinical trial in the first half of 2019. We do not intend to initiate the second Phase 3 clinical trial until we review and discuss with the FDA the data from the first Phase 3 clinical trial. Given the anticipated use of OTX-TP as a chronic therapy, we intend to generate six-month (300 patients) and one-year (100 patients) safety data to support our product registration. In order to help meet these targets, we began enrollment in the open-label one-year safety extension study in July 2018.

### ***OTX-TIC (intracanalicular travoprost implant)***

OTX-TIC is our product candidate for glaucoma patients in need of a more significant reduction in IOP and ocular hypertension. 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. Preclinical studies to date have demonstrated reduction of IOP and pharmacokinetics in the aqueous humor that suggest a pharmacodynamic response of IOP reduction in humans. Our investigational new drug application, or IND, for our U.S. trial became effective in the first quarter of 2018. We initiated an open-label, proof-of-concept Phase 1 clinical trial in the United States in the second quarter of 2018, with our first patient having been dosed more than nine months ago. This clinical trial is a multi-center, open-label, dose-escalation, proof-of-concept study designed to evaluate the safety, durability, tolerability, and efficacy of OTX-TIC in patients with primary open-angle glaucoma or ocular hypertension. We anticipate presenting initial results from this clinical trial at the Association of Research and Vision of Ophthalmology meeting in April 2019.

### ***Back-of-the-Eye Programs***

We are engaged in the development of formulations 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 initial development efforts are focused on the use of our local programmed-release hydrogel in combination with anti-angiogenic drugs, such as protein-based anti-VEGF drugs, or small molecule drugs, such as TKIs, for the treatment of retinal diseases such as wet AMD, retinal vein occlusion and diabetic macular edema. Our initial goal for these programs is to provide programmed release delivery over a four to nine month period thereby reducing the frequency of the current monthly or bi-monthly intravitreal injection regimen for wet AMD and other retinal diseases and providing a more consistent uniform release of drug over the treatment period.

### ***OTX-TKI (intravitreal tyrosine kinase inhibitor implant)***

OTX-TKI is a preformed, bioresorbable hydrogel fiber incorporating a small molecule TKI with anti-angiogenic properties delivered by intravitreal injection. TKIs have shown promise in the treatment of wet AMD. In May 2017, we reported data from preclinical studies evaluating the efficacy, tolerability and pharmacokinetics of OTX-TKI. In this study, OTX-TKI was well-tolerated, and high levels of drug were maintained in the tissue for up to twelve months in Dutch belted rabbits. In the first quarter of 2019, we dosed two patients in a Phase 1 clinical trial in Australia. This clinical trial is a multi-center, open-label study designed to evaluate the safety, durability and tolerability of OTX-TKI for up to nine months. We also plan to evaluate biological activity by following visual acuity over time and measuring retinal thickness using standard optical coherence tomography.

### ***OTX-IVT (intravitreal aflibercept implant) in Collaboration with Regeneron***

In October 2016, we entered into a strategic collaboration, option and license agreement, or Collaboration Agreement, with Regeneron for the development and potential commercialization of products using our hydrogel 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. Under the terms of the 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 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 have 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. A joint research committee comprised of an equal number of representatives from each of Regeneron and us is responsible for reviewing, approving and overseeing the parties' research and development activities with respect to licensed product candidates and making any modifications to those activities. In general, Regeneron has final decision-making authority over matters on which the joint research committee deadlocks, following escalation to designated executive officer representatives of the parties, except for matters that would impose a material increase in costs or obligations on us beyond those costs and obligations included in the mutually agreed collaboration plan. We refer to the formulation we are developing with Regeneron as OTX-IVT.

Regeneron is responsible for funding an initial preclinical tolerability study, which it initiated in early 2018. If the Option is exercised, Regeneron will 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 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. The option is exclusive until 12 months after Regeneron has received a product candidate in accordance with a collaboration plan and non-exclusive for an additional six months following the end of the exclusive period. In December 2017, we delivered to Regeneron the final formulation for Regeneron's initial preclinical tolerability study. Although we are engaged in ongoing discussions with Regeneron, Regeneron has not informed us of its decision to exercise the Option. Pending a decision from Regeneron, we are not actively pursuing further formulation development or other preclinical testing under the Collaboration Agreement. We are also eligible to receive up to \$145 million per Licensed Product upon the achievement of specified development and regulatory milestones, including successful results from the first-in-human clinical trial, \$100 million per Licensed Product upon first commercial sale of such Licensed Product and up to \$50 million based on the achievement of specified sales milestones for all 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 Licensed Products.

#### *ReSure® Sealant*

Following our receipt of FDA approval for ReSure Sealant, we commercially launched this product in the United States in 2014. ReSure Sealant is approved to seal corneal incisions following cataract surgery and is the first and only surgical sealant to be approved by the FDA for ophthalmic use. 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. While ReSure Sealant remains commercially available in the United States, there is no sales support currently provided to the product at this time. We have received only limited revenues from ReSure Sealant to date and do not anticipate sales for 2019 to be material.

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 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 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. 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. We have provided regular periodic reports to the FDA on the progress of this post-approval study.

We received a warning letter from the FDA in October 2018 relating to our compliance with data collection and information reporting obligations in the Device Exposure Registry Study. The FDA warning letter refers to a lack of progress with the enrollment and related data collection and information reporting obligations for a required post-approval trial. In November 2018, we appealed this warning letter. In December 2018, the FDA rejected our appeal. 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. We continue to work with FDA to find a path to evaluate the incidence of endophthalmitis in patients receiving ReSure Sealant. ReSure Sealant currently remains commercially available in the United States, though there is no sales support provided to the product at this time.

### *Additional Potential Areas for Growth*

In addition to our focus on formulating, developing and commercializing innovative therapies for diseases and conditions of the eye, we are also assessing the potential use of our hydrogel platform technology in other areas of the body.

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 amends and restates in full the Company's prior amended and restated license agreement with Incept, dated as of January 27, 2012, to expand the scope of the Company's 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 product 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 product candidates, our intracameral product candidates, our intravitreal implant product candidates, 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.

Our product candidates target large and growing markets. Allied Market Research estimates that the annual worldwide market for ophthalmic medications was \$29 billion as of 2016 and is expected to increase to \$42.7 billion by 2023.

We have in-licensed all of the patent rights and a significant portion of the technology for ReSure Sealant and our hydrogel platform technology product candidates from Incept, LLC, or Incept, an intellectual property holding company. Amarpreet Sawhney, our former President and Chief Executive Officer and current Chairman of the Board of Directors, is a general partner of Incept and has a 50% ownership stake in Incept.

Our founders and management team have significant experience in developing and commercializing medical products for other companies using bioresorbable hydrogel technology, including FDA-approved and currently marketed medical products such as DuraSeal Dural Sealant\* (marketed by Integra Lifesciences, Inc.), a sealant for cranial and spine surgery, and Mynx\* (marketed by Cardinal Health, Inc.), a sealant for femoral artery punctures after angiography and angioplasty. Dr. Sawhney was the founder, President and Chief Executive Officer of Confluent Surgical, Inc., the company that developed and commercialized the DuraSeal Dural Sealant and was the technology founder of AccessClosure, Inc., the company that developed and commercialized Mynx.

### *Product Pipeline*

The following table summarizes the status of our key product development programs and 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.

PRODUCT/PROGRAM	DISEASE STATE	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	REGULATORY APPROVAL
<b>INTRACANALICULAR INSERTS</b>						
<b>Dextenza®</b> (dexamethasone ophthalmic insert) 0.4mg	Post-surgical pain					
<b>Dextenza®</b> (dexamethasone ophthalmic insert) 0.4mg	Inflammation					
<b>Dextenza®</b> (dexamethasone ophthalmic insert) 0.4mg	Allergic conjunctivitis					
<b>OTX-TP</b> (travoprost insert)	Glaucoma and ocular hypertension					
<b>OTX-BPI</b> (bupivacane)	Acute Ocular Pain					
<b>OTX-BSI</b> (besifloxacin & dexamethasone)	Post-op pain, inflammation & anti-bacterial					
<b>OTX-KTO</b> (ketotifen)	Allergy					
<b>OTX-CSI</b> (cyclosporine)	Chronic dry eye					
<b>INTRACAMERAL IMPLANT</b>						
<b>OTX-TIC</b> (travoprost implant)	Glaucoma and ocular hypertension					
<b>INTRAVITREAL IMPLANTS</b>						
<b>OTX-TKI</b> (tyrosine kinase inhibitor implant)	Wet AMD, DME and RVO					
<b>OTX-IVT*</b> (anti-VEGF antibody implant)	Wet AMD, DME and RVO					
<b>OCULAR SEALANT</b>						
<b>ReSure®</b> SEALANT	Cataract incision closure					

\* In Partnership with REGENERON

† Wet Age-related Macular Degeneration (Wet AMD), Diabetic Macular Edema (DME), Retinal Vein Occlusion (RVO)

## 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:

- Launch the commercialization of **DEXTENZA®** (dexamethasone ophthalmic insert) 0.4mg for intracanalicular use for the treatment of ocular pain following ophthalmic surgery. DEXTENZA is the first FDA-approved intracanalicular insert delivering dexamethasone to treat post-surgical ocular pain for up to 30 days with a single administration. We are building a highly-focused, key account manager sales force that will initially target the highest volume cataract surgery centers. We applied for a C-code for transitional payment status on November 30, 2018 and expect to receive a reimbursement code in the middle of 2019.
- Create proprietary solutions for ophthalmic diseases and conditions based on our bioresorbable hydrogel technology platform's ability to improve the delivery of FDA-approved therapeutic agents. We are directing the majority of our development efforts towards applying our proprietary PEG-based bioresorbable hydrogel technology platform to product candidates that are designed to provide local programmed-release of therapeutic agents to the eye using active pharmaceutical ingredients that are currently used in ophthalmic drugs approved by the FDA and that are or are expected to become available on a generic basis prior to anticipated launch dates or to which we have access through our existing collaboration with Regeneron or in any future collaborations. Our technology uses a proprietary composition of PEG to make bioresorbable

hydrogels that we specifically engineer for each of our product candidates. By focusing on the development of products based on FDA-approved therapeutic agents, we believe that we can advance potential products efficiently and predictably through the development cycle based on well-defined clinical and regulatory approval pathways. We believe this strategy of selecting FDA-approved therapeutic agents and improving their delivery represents an attractive risk-reward profile relative to new drug development.

- *Complete clinical development of and seek marketing approval for our most advanced intracanalicular insert product candidates for diseases and conditions of the front of the eye.*
  - *Post-Surgical Inflammation.*
    - § We filed an sNDA for DEXTENZA for post-surgical ocular inflammation in January 2019. We expect the FDA to complete its review of this submission in the second half of 2019 and, if approved, intend to add this expanded indication to the label of our currently approved DEXTENZA product for post-surgical ocular pain.
  - *Glaucoma.*
    - § With regard to OTX-TP, we initiated the first of two Phase 3 trials of our travoprost insert for the treatment of glaucoma and ocular hypertension in September 2016 and expect topline efficacy data in the first half of 2019. We anticipate discussing the results of this first Phase 3 clinical trial with the FDA prior to initiating a second Phase 3 clinical trial. Given the anticipated use of OTX-TP as a chronic therapy, we have also commenced a data safety study to help generate six-month (300 patients) and one year (100 patients) safety data to support our product registration.
    - § We are also advancing OTX-TIC, our travoprost-based intracameral implant for the treatment of moderate to severe glaucoma and ocular hypertension for four to six months. We initiated an open-label, proof-of-concept Phase 1 clinical trial in the United States in the second quarter of 2018, with our first patient having been dosed more than nine months ago. We intend to announce preliminary results from this trial during the first half of 2019.
- *Apply our local programmed-release intracanalicular insert technology for the treatment of additional diseases and conditions of the front of the eye.* We intend to apply our proprietary PEG-based bioresorbable hydrogel technology platform to product candidates that are designed to provide local programmed-release of therapeutic agents to the eye using active pharmaceutical ingredients that are currently used in ophthalmic drugs approved by the FDA and that are or are expected to become available on a generic basis prior to anticipated launch dates. Our technology uses a proprietary composition of PEG to make bioresorbable hydrogels specifically engineered for placement in the intracanalicular for each of our product candidates. By focusing on the development of products based on FDA-approved therapeutic agents, we believe that we can advance potential products efficiently and predictably through the development cycle based on well-defined clinical and regulatory approval pathways. We believe this strategy represents an attractive risk-reward profile relative to new drug development. We currently have a number of preclinical programs that we are pursuing including OTX-BPI for acute ocular pain; OTX-BSI for post-operative; inflammation and bacterial infection; OTX-KTO for allergy; and OTX-CSI for chronic dry-eye.

In addition to these preclinical development programs, we have also completed two Phase 3 clinical trials for the use of DEXTENZA to treat allergic conjunctivitis. We expect to initiate a third Phase 3 clinical trial in the second half of 2019 for this program.
- *Pursue development of our intravitreal implant and other technologies for back-of-the-eye diseases and conditions.* We are developing OTX-TKI, a hydrogel implant, designed to release anti-angiogenic drugs, including anti-VEGF formulations, over a sustained period following administration by an intravitreal injection to address the large and growing markets for diseases and conditions of the back of the eye, including wet AMD. Our goal for this intravitreal product candidate is to provide local programmed-release of the anti-angiogenic drugs up to a nine month period, thereby reducing the frequency of the current

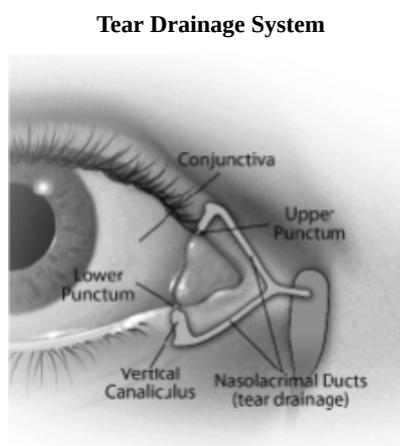
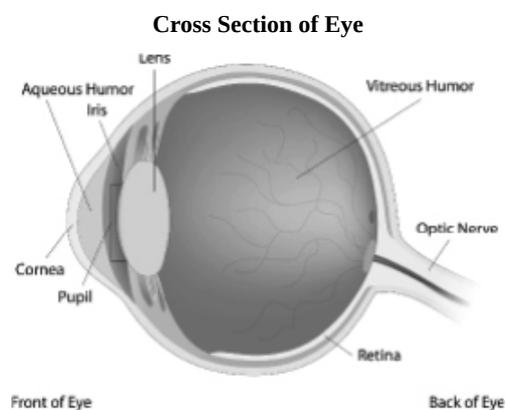
monthly or bi-monthly intravitreal injection regimen. We believe that less frequent injections will be more convenient for patients and may reduce the risk of infection and other potential side effects associated with each injection. We also believe that our hydrogel implant could potentially provide a more consistent level of therapeutic agent compared with existing therapies. In the first quarter of 2019, we dosed two patients in an open-label proof-of-concept Phase 1 clinical trial of OTX-TKL. This Phase 1 clinical trial is being conducted in Australia.

In October 2016, we entered into the Collaboration Agreement with Regeneron for the development and potential commercialization of products containing our extended-delivery hydrogel 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.

- *Utilize our hydrogel platform to enable local programmed-release of therapeutics to areas of the body outside the eye.* In September 2018, we entered into the Second Amended Agreement with Incept to expand 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. We intend to explore programs outside of the eye not only on our own but also potentially through partnerships or collaborations with third parties who have expertise and experience with other therapeutics as well as other areas of the body.

## Eye Disease

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. 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. Diseases and conditions affecting the front of the eye are generally treated either with surgery or with medications delivered to the ocular surface by eye drops. Intravitreal injections or oral pills are typically used to deliver medications to the back of the eye.



## Front-of-the-Eye Diseases and Conditions

### *Ocular Pain and Inflammation*

Ocular pain and inflammation are common conditions caused by a variety of factors, including ophthalmic surgery, allergic conjunctivitis and dry eye disease.

### *Post-Surgical Ocular Pain and Inflammation*

Ocular pain and inflammation 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 Scope has estimated that approximately 5.8 million ocular surgeries were to be performed in the United States in 2018.

### *Allergic Conjunctivitis*

Allergic conjunctivitis 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.

### *Dry Eye Disease*

Dry eye disease affects the ocular surface and is characterized by dryness, inflammation, pain, discomfort and irritation. 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 for the treatment of moderate to severe dry eye disease consists of Restasis for increasing tear production, marketed by Allergan, lifitegrast, for the treatment of the signs and symptoms of dry eye disease, marketed by Shire under the brand name Xiidra and off-label use of corticosteroids. Based on our review of industry sources, we estimate that approximately 20 million people in the United States have dry eye disease, including approximately five million people who suffer from moderate to severe dry eye disease.

### *Market Data*

According to IMS Health data, approximately 20.3 million prescriptions were filled in the United States in 2018 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 8.4 million prescriptions and \$723 million in sales for single-agent corticosteroids, 3.3 million prescriptions and \$369 million in sales for NSAIDs, 4.6 million prescriptions and \$282 million in sales for corticosteroid and antibiotic combination products and approximately 4.0 million prescriptions and \$2.7 billion in sales of Restasis and Xiidra for dry eye disease. According to IMS Health data, approximately 6.8 million anti-allergy eye drop prescriptions were filled in the United States in 2018, resulting in sales of approximately \$477 million. The steroid market for eye drops to treat ocular diseases and conditions 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.

### *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.

In a healthy eye, fluid is continuously produced and drained to maintain pressure equilibrium and provide nutrients to the ocular tissue. Excess fluid production or insufficient drainage of fluid in the front of the eye or a combination of these problems causes increased IOP. The increased IOP associated with uncontrolled glaucoma results in degeneration of the optic nerve in the back of the eye and loss of peripheral vision. Once glaucoma develops, it is a chronic condition that requires life-long treatment. According to the Glaucoma Research Foundation, approximately 3.0 million people in the United States suffer from glaucoma. Open-angle glaucoma, in which the space between the iris and the cornea through which fluid drains is relatively wide, is the most common form of glaucoma. According to the Glaucoma Research Foundation, open-angle glaucoma accounts for at least 90% of all glaucoma cases.

To lower IOP, physicians typically initiate treatment by prescribing drugs administered as eye drops. These drugs either decrease fluid production or enhance fluid drainage. The classes of topical drugs used to treat glaucoma include prostaglandin analogs, or PGAs, beta-blockers, alpha-adrenergic agonists and carbonic anhydrase inhibitors. PGAs are the most widely prescribed class of drugs for glaucoma and are considered first-line glaucoma treatment. PGAs reduce IOP by enhancing the clearance and drainage of ocular fluid. The most frequently prescribed PGA is once-daily latanoprost, although travoprost, unoprostone and bimatoprost are also frequently used in the management of open-angle glaucoma. In cases where glaucoma is not easily managed by a drug regimen, surgical or laser treatments may be undertaken.

#### *Market Data*

According to IMS Health data, approximately 35.2 million prescriptions were filled in the United States in 2018 for drugs administered by eye drops for the treatment of glaucoma, resulting in sales of approximately \$3.1 billion. A typical prescription provides approximately one month of treatment. We expect prescription volume to grow, in large part as a result of the aging population. According to IMS Health, PGAs accounted for approximately half of the prescription volume in the glaucoma market in 2018. 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.

#### ***Bacterial Infection***

Bacterial conjunctivitis is one of the most common forms of ocular infection. It is an inflammatory disease of the eye caused by infection with bacteria such as Haemophilus influenzae, Streptococcus pneumoniae or Staphylococcus aureus. While bacterial conjunctivitis typically resolves on its own over time, it is often treated with antibiotics which can speed recovery, reduce relapse and potentially prevent important sight-threatening complications.

#### *Market Data*

According to IMS Health data, approximately 16.5 million prescriptions were filled in the United States in 2018 for ophthalmic antibiotics administered by eye drops, resulting in sales of approximately \$428 million.

#### **The Use of Eye Drops and their 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.

### **Back-of-the-Eye Diseases and Conditions**

There are a range of back-of-the-eye diseases and conditions that adversely affect vision. One of the principal back-of-the-eye conditions 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 are 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 a study on the burden of AMD published in 2006 in the peer-reviewed journal *Current Opinion in Ophthalmology*, approximately 1.2 million people in the United States suffer from wet AMD. In addition, AMD Alliance International reports that approximately 200,000 new cases of wet AMD arise each year in the United States. The incidence of wet AMD increases substantially with age, and we expect that the number of cases of wet AMD will increase with growth of the elderly population in the United States. The anti-VEGF market for the treatment of wet AMD consists predominantly of two drugs that are approved for marketing and primarily prescribed for the treatment of wet AMD, Lucentis marketed in the United States by Genentech and Eylea marketed in the United States by Regeneron, and off-label use of the cancer therapy Avastin. In 2018, sales of Lucentis and Eylea totaled approximately \$5.8 billion in the United States and \$10.3 billion globally.

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.

## **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 2018 there were to be approximately 4.2 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. An additional visit may be required to remove sutures, thus adding time, inconvenience and expense to the surgical process. Sutures may also lead to astigmatism, a distortion of the cornea. 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**

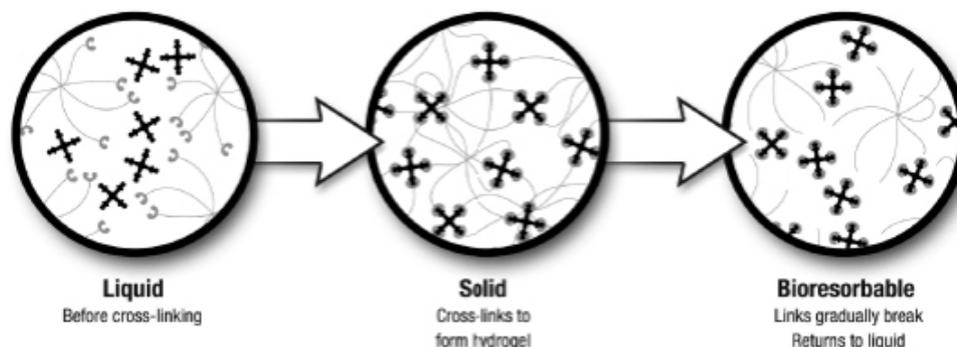
### ***Our Hydrogel Technology Platform***

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 founders have previously used this same hydrogel technology to develop FDA-approved and currently marketed medical products for other companies such as DuraSeal Dural Sealant® (marketed by Integra Lifesciences, Inc.), a sealant for cranial and spine surgery, and Mynx® (marketed by Cardinal Health), a sealant for femoral artery punctures after angiography and angioplasty.

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 have used bioresorbable hydrogels to engineer each of our intracanalicular insert product candidates, our intracameral implant product candidates, ReSure Sealant and our intravitreal implant product candidates.

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

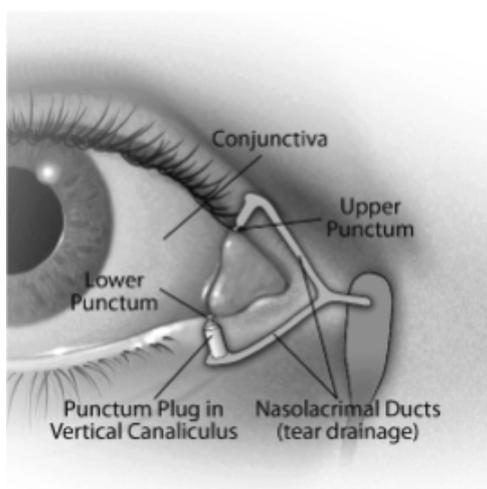
degradation rate. Our technology enables us to make hydrogels that can bioresorb over days, weeks or several months. The figure below depicts the formation and bioresorption of the hydrogel for ReSure Sealant.



***Intracanalicular Insert-Based Local Programmed-Release Therapies for Front-of-the-Eye Diseases and Conditions***

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.

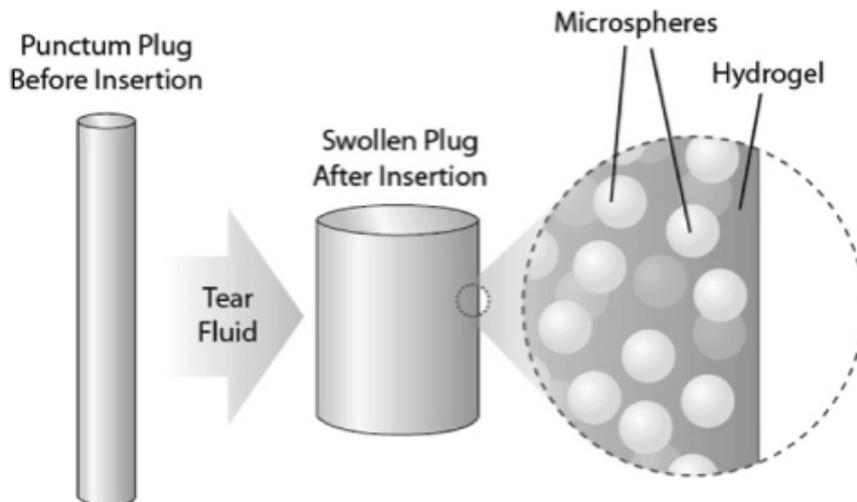
Our inserts allow incorporation of a variety of drugs with a controllable range of delivery durations and delivery rates. For acute conditions, such as post-surgical ocular pain and inflammation and allergic conjunctivitis, we have

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.

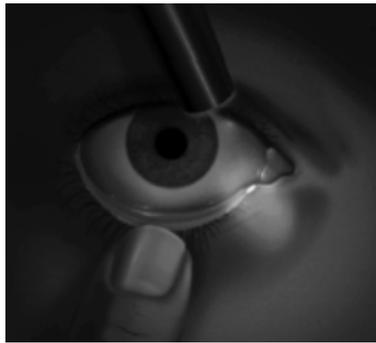
We manufacture our intracanalicular inserts from dried PEG-based hydrogel formed into tiny rods that hold an active pharmaceutical ingredient in a preservative-free formulation. We embed the active pharmaceutical ingredient in the pre-hydrogel liquid formulation, which then solidifies to form a hydrogel 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;
- 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.

### *Anticipated Benefits of Our Intracanalicular Inserts Compared to Eye Drops*

We believe our intracanalicular insert product candidates may offer a range of favorable attributes as compared to eye drops, including:

- *Improved patient compliance.* Our intracanalicular inserts are inserted 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 intracanalicular inserts dissipate over time and do not require removal for acute conditions or frequent removal for chronic conditions, we believe our intracanalicular inserts address the problem of patient compliance.
- *Ease of administration.* We have designed our intracanalicular inserts 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 intracanalicular inserts to deliver drug in a programmed fashion to the surface of the eye 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 administrations. Further, we are designing our 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 intracanalicular inserts are designed to fully dissipate over a period of two to three times the length of the expected period of release of the therapeutic agent and can be removed if necessary by a healthcare professional.
- *Avoidance of preservative side effects.* Our intracanalicular inserts 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.

### *Intravitreal Implants for Back-of-the-Eye Diseases and Conditions*

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 initial development efforts are focused on the use of our programmed-release hydrogel in combination with anti-angiogenic drugs such as protein-based anti-VEGF drugs or small molecule drugs, such as TKIs for the treatment of retinal diseases, such as wet AMD, retinal vein occlusion and diabetic macular edema. Our initial goal for these programs is to provide extended delivery of a protein-based large molecule or small molecule TKI drug targeting VEGF and other targets over a four to six month period following administration of a bioresorbable hydrogel incorporating the drug by an injection into the vitreous humor, thereby reducing the frequency of the current monthly or bi-monthly intravitreal injection regimen for wet AMD and other retinal diseases and potentially providing a more consistent, uniform release of drug over the treatment period.

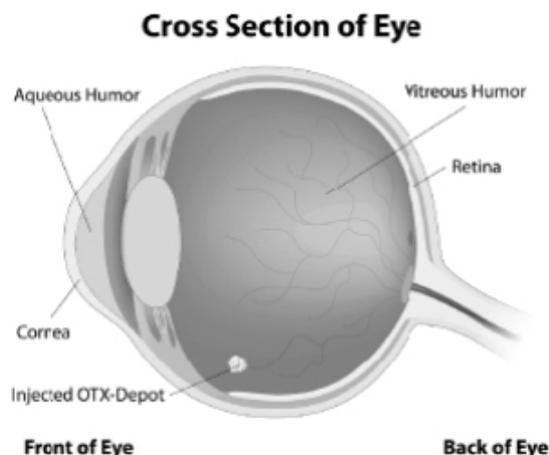
We are pursuing a multi-pronged strategy to seek to maximize the potential of this technology.

- We are researching the delivery of small molecule TKIs from our hydrogel implant and we initiated an open-label, proof-of-concept Phase 1 clinical trial in Australia in the first quarter of 2019. This clinical trial is a multi-center, open-label study designed to evaluate the safety, durability and tolerability of OTX-TKI for up to nine months. We have conducted preclinical work on this compound and have achieved local programmed-release and pharmacodynamic effect *in vivo* for up to twelve months. We believe this class of drugs 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, these drugs 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 little short half-lives in solution. We believe our local drug delivery technology gives us potential advantages in this regard. 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.

- We are also evaluating an intravitreal implant through our collaboration with Regeneron, consisting of a PEG-based hydrogel matrix containing embedded micronized particles of aflibercept. Aflibercept is marketed by Regeneron under the brand name Eylea. We designed the injection to be delivered to the vitreous chamber of the eye using a fine gauge needle. We entered into the Collaboration Agreement with Regeneron in October 2016 for the development and commercialization of protein-based anti-VEGF drugs, with the initial product candidate incorporating the drug aflibercept into our hydrogel. As previously discussed, pending a decision from Regeneron, we are not actively pursuing further formulation development or other preclinical testing.

Our intravitreal implant consists of a PEG-based hydrogel suspension, which contains embedded micronized protein particles of an anti-angiogenic compound. 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.



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.

#### ***ReSure Sealant for Ocular Wound Closure***

ReSure Sealant is our bioresorbable hydrogel product 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.

We commercially launched ReSure Sealant in February 2014 on a region-by-region basis in the United States through a network of independent distributors. In early 2017, we terminated these distributors and hired a contract sales force of four representatives to sell ReSure Sealant. In July 2017, in connection with a broader reduction in force, we terminated these representatives. At this time, we have no sales support provided to ReSure Sealant, and we have no plans to hire a sales force to focus on this product. We also believe that the market opportunity for a surgical sealant following cataract surgery may be modest because sutures are used in only approximately 14% of cataract surgeries and, currently, there is no direct reimbursement for ReSure Sealant. As a result, we do not expect to generate meaningful levels of revenue from the sale of ReSure in 2019.

**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.

<u>Product / Program</u>	<u>Indication</u>	<u>Description (Active Pharmaceutical Ingredient)</u>	<u>Stage of Development</u>	<u>Status</u>
<b>Approved Product</b>				
DEXTENZA	Post-surgical ocular pain	Intracanalicular insert (Dexamethasone)	Approved for post-surgical ocular pain	Approved by the FDA in November 2018; product will be commercially launched upon the receipt of a C-code for transitional pass through payment; receipt of the C-code anticipated in the middle of 2019
ReSure Sealant	Cataract incision closure	Ocular sealant	Marketed	Approved by the FDA in January 2014; commercially launched in the United States in February 2014. In October 2018, we received a FDA warning letter and we appealed in November 2018. The appeal was rejected in December 2018. We continue to work with FDA.
<b>Late Stage Clinical Product Candidates</b>				
DEXTENZA	Post-surgical inflammation	Intracanalicular insert (Dexamethasone)	Phase 3	sNDA submission for post-surgical ocular inflammation in January 2019
DEXTENZA	Allergic conjunctivitis	Intracanalicular insert (Dexamethasone)	Phase 3	Phase 2 trial completed in November 2014; topline results from the two Phase 3 trials; first Phase 3 trial reported in October 2015 and second Phase 3 trial reported in June 2016; a third Phase 3 trial is expected to commence in the second half of 2019
OTX-TP	Glaucoma	Intracanalicular insert (Travoprost)	Phase 3	Phase 2a trial completed in May 2014; Phase 2b topline results reported in October 2015; initiated the first of two Phase 3 clinical trials in September 2016; topline data from the first Phase 3 trial expected in the first half of 2019

<b>Product / Program</b>	<b>Indication</b>	<b>Description (Active Pharmaceutical Ingredient)</b>	<b>Stage of Development</b>	<b>Status</b>
<b>Early Stage Clinical Product Candidates</b>				
OTX-TIC	Glaucoma and ocular hypertension	Intracameral implant (Travoprost)	Phase 1	Initiated a Phase 1 clinical trial outside of the U.S. in the third quarter of 2017 which has since been closed due to lack of enrollment; initiated a new Phase 1 clinical trial in the first half of 2018 in the U.S. with initial results at the Association of Research and Vision of Ophthalmology meeting in April 2019
OTX-BPI	Acute ocular pain	Bupivacane	Preclinical	Ongoing preclinical studies
OTX-BSI	Post-operative pain, inflammation & antibacterial	Besifloxacin and dexamethasone	Preclinical	Ongoing preclinical studies
OTX-KTO	Allergy	Ketotifen	Preclinical	Ongoing preclinical studies
OTX-CSI	Chronic dry eye	Cyclosporine	Preclinical	Ongoing preclinical studies
Anti-angiogenic hydrogel implants				
OTX-TKI	Wet AMD	Intravitreal implant (Tyrosine kinase inhibitor anti-angiogenic compound)	Phase 1	Initiated a Phase 1 clinical trial in Australia in the second half of 2018
OTX-IVT	Wet AMD DME and RVO	Intravitreal implant (Protein-based anti-angiogenic compound)	Preclinical	Preclinical studies

### **Dexamethasone Intracanalicular Insert**

Our DEXTENZA (local programmed-release dexamethasone) intracanalicular insert product candidate incorporates the corticosteroid dexamethasone as an active pharmaceutical ingredient in our proprietary hydrogel insert. We are developing DEXTENZA for the treatment of post-surgical ocular pain and inflammation and allergic conjunctivitis. We have designed DEXTENZA to deliver therapeutic levels of dexamethasone over a period of approximately 30 days. We have reported topline results from three Phase 3 clinical trials for the treatment of post-surgical ocular pain and inflammation and two Phase 3 clinical trials for the treatment of allergic conjunctivitis.

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 pain and inflammation following ocular surgery;
- is available from multiple qualified suppliers; and
- has physical properties that are well suited for incorporation within our intracanalicular inserts.

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 pain and inflammation 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.

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, have limited its widespread adoption as a treatment for the treatment of allergic conjunctivitis. These spikes 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. We believe, based on our clinical trial results to date, that periodic use of the DEXTENZA for allergic conjunctivitis will 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.

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 standard 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. As with allergic conjunctivitis, there are safety limitations associated with the use of corticosteroids for dry eye disease that have limited wide spread adoption. We believe that DEXTENZA has potential as a short-term therapy for more severe cases of dry eye caused by inflammation, followed by the delivery of an immunosuppressant drug such as cyclosporine after the inflammation has been reduced.

#### ***Overview of DEXTENZA Clinical Development***

We are conducting clinical development of DEXTENZA for the treatment of post-surgical ocular pain and inflammation and allergic conjunctivitis. The following summarizes our clinical development to date for DEXTENZA.

- In March and April 2015, we reported topline results from two Phase 3 clinical trials for the treatment of post-surgical ocular pain and inflammation. 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 pain and inflammation. 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 pain and inflammation 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 CRL from the FDA regarding our NDA for DEXTENZA. This CRL pertained to deficiencies in manufacturing process and controls identified during a pre-NDA approval inspection of our manufacturing facility. In January 2017, we resubmitted our NDA to the FDA. Following a re-inspection of manufacturing operations by the FDA which was completed in May 2017, we received an FDA Form 483 containing inspectional observations focused on manufacturing processes and analytical testing related to the manufacture of drug product for commercial production. In July 2017, we received a CRL from the FDA regarding our NDA for DEXTENZA for the treatment of post-surgical ocular pain. The FDA concerns included deficiencies in manufacturing processes and analytical testing related to manufacturing of drug product identified during the pre-NDA approval inspection. 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 November 2014, we completed a Phase 2 clinical trial evaluating the safety and efficacy of DEXTENZA for the treatment of allergic conjunctivitis. Based upon the encouraging results of this Phase 2 clinical trial and a subsequent meeting with the FDA, we began enrollment for an initial Phase 3 clinical trial of DEXTENZA for this indication in June 2015. We announced topline results from this trial in October 2015. We initiated a second Phase 3 clinical trial of DEXTENZA for this indication in November 2015. We announced topline results for the second Phase 3 clinical trial in June 2016.
- In January 2015, we initiated a Phase 2 exploratory clinical trial of DEXTENZA for the treatment of dry eye disease. We reported topline results from this trial in December 2015. We are not currently pursuing DEXTENZA for the treatment of dry eye disease.

### ***Clinical Trials for Post-Surgical Ocular Pain and Inflammation***

#### ***Completed Phase 2 Clinical Trial***

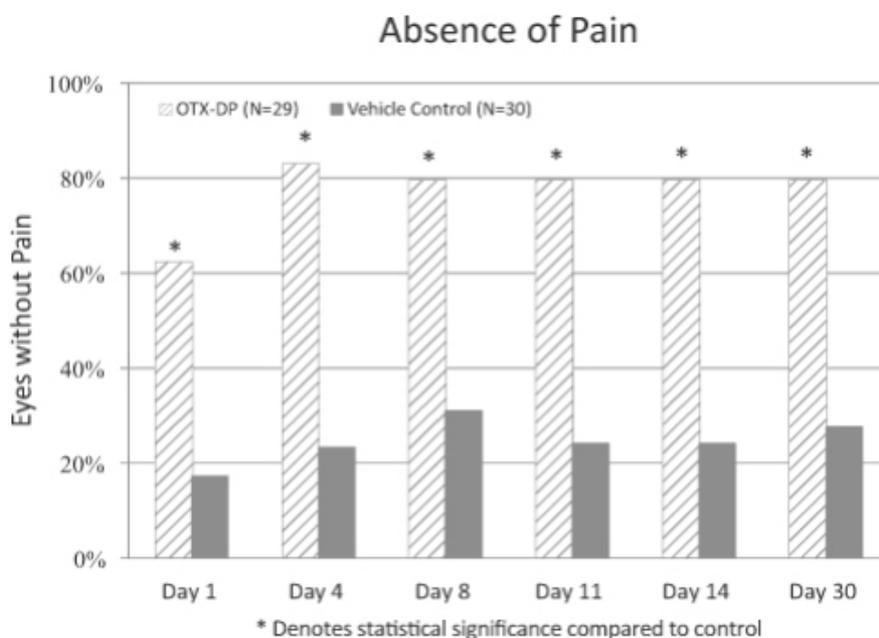
In 2013, we completed a prospective, randomized, parallel-arm, vehicle-controlled, multicenter, double-masked Phase 2 clinical trial evaluating the safety and efficacy of DEXTENZA for the treatment of ocular pain and inflammation following cataract surgery. We conducted this trial in 60 patients at four sites in the United States pursuant to an effective IND. We randomized patients in a 1:1 ratio to receive either DEXTENZA or a placebo vehicle control intracanalicular insert without active drug. One patient randomized into the DEXTENZA group was excluded from the trial because the investigator was unable to insert the insert, resulting in 29 patients in the DEXTENZA group and 30 patients in the vehicle control group. We evaluated patients in this trial at days 1, 4, 8, 11, 14 and 30 following surgery.

One of our goals for this trial was to determine the appropriate primary endpoints for a subsequent Phase 3 clinical development program. The two primary efficacy measures in this trial were absence of inflammatory cells in the anterior chamber of the study eye and absence of pain in the study eye. When viewed with a slit lamp biomicroscope, these inflammatory cells, referred to as cells in a slit lamp examination, appear like dust specks floating in a projected light beam. The presence of these cells in the anterior chamber indicates inflammation. In this trial, 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 was the difference in the proportion of patients in each treatment group with absence of cells in the anterior chamber of the study eye at day 8 following surgery. The second primary efficacy endpoint 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.

We evaluated as secondary measures the absence of flare in the anterior chamber of the study eye at each evaluation date, 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 day 8 and insert retention and visualization. Flare is a scattering of light in the aqueous humor when viewed during a slit lamp biomicroscopic examination. Flare occurs when the protein content of the aqueous humor increases due to intraocular inflammation.

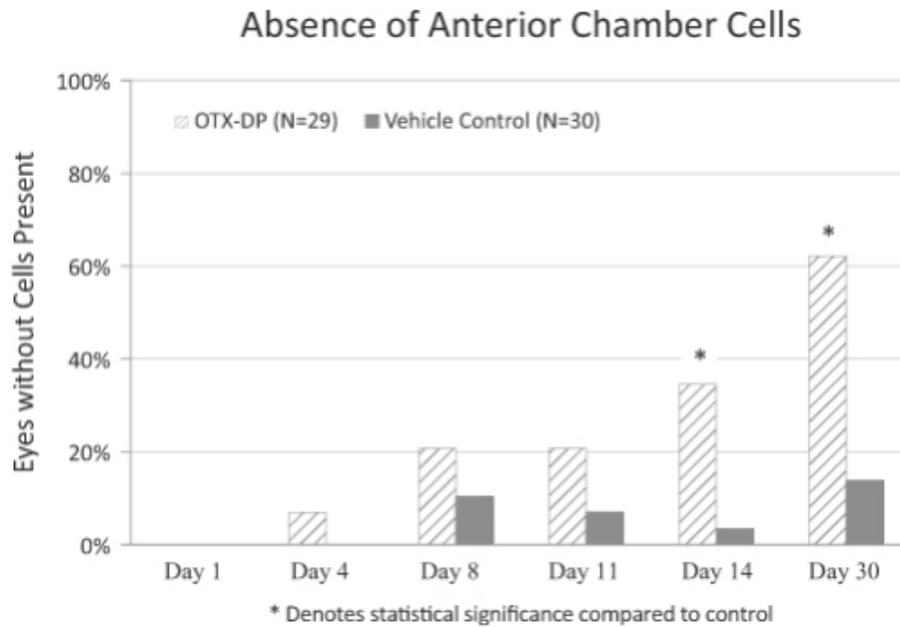
We enrolled patients in this trial who were at least 21 years of age undergoing unilateral clear corneal cataract surgery. We excluded patients from the trial if, among other reasons, they had intraocular inflammation or ocular pain in the study eye at screening or had glaucoma or ocular hypertension.

**Efficacy:** In this trial, DEXTENZA met the primary efficacy endpoint with statistical significance for absence of pain compared to the vehicle control at day 8 ( $p < 0.0001$ ). 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. The differences between DEXTENZA and the vehicle control for absence of pain also were statistically significant at each other evaluation date ( $p < 0.0002$ ). These results are shown in the graph below. In this graph and other graphs appearing further below, we use the abbreviation “N” to reference the number of patients in each group.

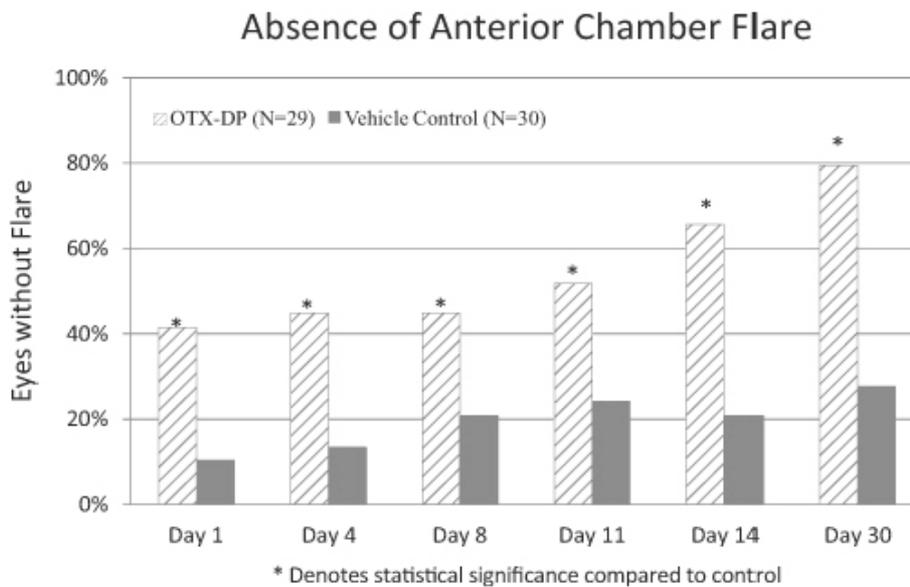


In this trial, DEXTENZA did not meet the primary efficacy endpoint with statistical significance for absence of cells in the anterior chamber compared to the vehicle control at day 8. However, there was a trend of improved absence

of anterior chamber cells at each evaluation date, with statistical significance at day 14 ( $p < 0.0027$ ) and day 30 ( $p < 0.0002$ ). These results are shown in the graph below.



Based on post hoc analysis, DEXTENZA showed statistical significance for absence of flare compared to vehicle control at each evaluation date. These results are shown in the graph below.



**Safety:** In this trial, there were three serious adverse events, none of which was considered related to the study treatment. The trial investigator determined the relatedness of the serious adverse events to study treatment based on his or her professional medical judgment and in accordance with the study protocol, which required the investigator to determine that a reasonable possibility did not exist that the study treatment caused the adverse event. None of the three serious adverse events: syncope, intracranial hemorrhage and cellulitis of the arm, were ocular in nature. In addition, there were a variety of adverse events in both the DEXTENZA group and the vehicle control group, with the adverse

events in the vehicle control group outnumbering the adverse events in the DEXTENZA group. In the DEXTENZA group, the only adverse event that occurred more than once was reduced visual acuity, which occurred twice. The most common adverse events in the vehicle control group were reduced visual acuity, conjunctival hyperemia and corneal edema. Overall, 19 adverse events were noted in the DEXTENZA group and 30 adverse events were noted in the vehicle control group. All adverse events were transient in nature and completely resolved by the end of the trial.

### *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 pain and inflammation 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.

### ***Regulatory Pathway***

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 CRL from the FDA regarding our NDA for DEXTENZA pertaining to deficiencies in manufacturing process and controls identified during a pre-NDA approval inspection. We resubmitted our NDA to the FDA in January 2017. Following a re-inspection of manufacturing operations by the FDA which was completed in May 2017, we received an FDA Form 483 containing inspectional observations focused on manufacturing processes and analytical testing related to the manufacture of drug product for commercial production. In July 2017, we received a CRL from the FDA regarding our NDA for DEXTENZA for the treatment of post-surgical ocular pain, which states that the FDA has determined that it cannot approve the NDA in its present form. In May 2017, we submitted our initial response to the Form 483 and, in November 2017, we submitted our responses to the FDA's remaining inspectional observations in an effort to close out the items identified in the Form 483.

We resubmitted our NDA for DEXTENZA for the treatment of post-surgical ocular pain in June 2018. 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. If we receive timely approval of the sNDA for post-surgical ocular inflammation, we expect to expand the labeling to include this indication. Although we conducted our Phase 3 clinical trials of DEXTENZA in patients who have undergone cataract surgery, these trials are intended to support a label for all post-surgical ocular surgeries.

### ***Clinical Trials for Allergic Conjunctivitis***

#### ***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 known as the Conjunctival Allergen Challenge model, or CAC™, which is a proprietary model owned by ORA, Inc., the clinical research organization we used to manage the trial. 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:

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

**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 initiated and completed two Phase 3 clinical trials.

#### *First Phase 3 Clinical Trial*

We initiated the first of these two 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 modified 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 is 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	Treatment		Treatment Difference (P-value)
		DEXTENZA	Vehicle	
Ocular Itching	3 min	1.68 (1.032)	2.66 (0.861)	-1.02 ( <b>&lt;0.0001</b> )
	5 min	1.87 (1.04)	2.74 (0.69)	-0.87 ( <b>&lt;0.0001</b> )
	7 min	1.70 (0.938)	2.74 (0.679)	-1.04 ( <b>0.0007</b> )
Conjunctival Redness	7 min	1.52 (0.641)	1.80 (0.764)	-0.26 ( <b>0.1082</b> )
	15 min	1.48 (0.698)	1.75 (0.786)	-0.32 ( <b>0.0419</b> )
	20 min	1.44 (0.710)	1.76 (0.766)	-0.29 ( <b>0.0667</b> )

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

**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.

### ***Regulatory Pathway***

We have completed two Phase 3 clinical trials evaluating DEXTENZA for the treatment of allergic conjunctivitis. We plan to conduct a third Phase 3 clinical trial commencing in the second half of 2019. Subject to obtaining favorable results from this third Phase 3 clinical trial, we plan to submit an sNDA to the FDA for DEXTENZA for the treatment of allergic conjunctivitis for only the ocular itching indication. We expect that we would submit this sNDA under Section 505(b)(2) of the FDCA. See “—Government Regulation—Section 505(b)(2) NDAs” for additional information. Based on discussions with the FDA, we expect to use safety results from our Phase 3 clinical trials of DEXTENZA for the treatment of post-surgical ocular pain and inflammation to support the sNDA for DEXTENZA for the treatment of allergic conjunctivitis.

### ***Clinical Trial for Dry Eye***

#### ***Phase 2 Clinical Trial***

In January 2015, we initiated a prospective, randomized, parallel-arm, vehicle-controlled, multicenter, bilateral, double-masked Phase 2 feasibility study evaluating the safety and efficacy of DEXTENZA for the treatment of dry eye disease. We enrolled 43 patients and evaluated 86 eyes at two sites in the United States pursuant to our effective IND. The clinical trial was not powered for statistical significance. We randomized patients in a 1:1 ratio to receive either DEXTENZA or a placebo vehicle control intracanalicular insert without active drug.

Designed as a serial phase exploratory study, patients were initially administered a placebo vehicle control intracanalicular insert for 45 days to establish a baseline for the investigational drug treatment. Patients who responded to the placebo insert in treatment of their dry eye disease were excluded from the trial. Patients who continued to exhibit symptoms of dry eye disease during the initial 45 days, as indicated by a minimum threshold of signs of corneal staining, were qualified for enrollment in the treatment phase of the trial. Qualified patients were then randomized to receive either DEXTENZA or a placebo vehicle control intracanalicular insert. Primary efficacy measures included corneal and conjunctival staining, tear osmolarity, tear film break-up time, presence of the insert, ease of product use and visualization, and resorption of the insert following therapy. We reported topline results for this clinical trial in December 2015.

In this exploratory Phase 2 clinical trial, patients were selected for a minimum threshold of signs of corneal staining and were randomized to either treatment with DEXTENZA or a placebo vehicle insert. Patients were stratified into groups based on the level of National Eye Institute aggregate corneal fluorescein staining score improvement and were then randomized into the treatment or placebo vehicle insert group per a pre-determined randomization list to maintain masking. DEXTENZA treated patients showed clinically meaningful benefits compared to patients receiving a placebo vehicle control intracanalicular insert, with improvement in total and inferior corneal staining as well as conjunctival staining. Total corneal staining at day 30 following randomization was significantly decreased from baseline in the DEXTENZA group (-3.14) compared to placebo (-1.10) ( $p=0.018$ ). Inferior staining showed clinically significant differences in the change from baseline in the DEXTENZA treatment group compared to the placebo group (-0.44 and -0.45 at day 15 and day 30, respectively). Corneal staining is a primary endpoint that has been used in recent Phase 3 dry eye clinical trials for dry eye disease conducted by other ophthalmology companies. Supportive analyses of lissamine green staining also demonstrated a clinically significant change in favor of DEXTENZA, where total staining was more than 1 point improved for the DEXTENZA group compared to the placebo group.

This clinical trial was designed to evaluate a range of objective and subjective measures (signs and symptoms, respectively) for DEXTENZA and was intended to explore which measures would be appropriate to include in the design of future clinical trials of DEXTENZA or other molecules in a sustained-release product as a potential therapy for

dry eye disease. Our long term strategy for the treatment of dry eye may be to use DEXTENZA as a mode of therapy to reduce inflammation in patients with acute dry eye conditions and pursue the development of an intracanalicular insert containing an immunosuppressant drug such as cyclosporine to treat chronic dry eye. Consequently, we are not currently pursuing DEXTENZA for the treatment of dry eye disease.

There was one serious adverse event in the DEXTENZA treatment group, myocardial infarction, that was not deemed to be treatment related. There were 17 adverse events in the DEXTENZA group and 11 adverse events in the vehicle control group. Eight patients in the DEXTENZA group reported 12 ocular related adverse events, and 4 patients in the vehicle control group reported 5 ocular related adverse events. Four patients in the DEXTENZA group reported 5 non-ocular related adverse events, and 5 subjects in the vehicle control group reported 6 non-ocular related adverse events. The most frequently reported ocular treatment related ocular adverse event was increased lacrimation, which was reported in 4 patients in the DEXTENZA group and 1 subject in the vehicle control group. Three patients, all from the DEXTENZA group, had a mild reduction in best corrected visual acuity, of which 2 were considered treatment related and 1 of these was not resolved during the trial.

### **Travoprost Intracanalicular Insert (OTX-TP)**

Our OTX-TP product candidate incorporates the PGA travoprost as an active pharmaceutical ingredient in our proprietary intracanalicular insert. We are developing OTX-TP for the treatment of glaucoma and ocular hypertension. We have completed a Phase 2a clinical trial of OTX-TP, and we reported topline efficacy results of a Phase 2b clinical trial of OTX-TP in the United States in October 2015. We are currently conducting the first of two Phase 3 trial of OTX-TP. In the first Phase 3 trial, we have completed target enrollment of 550 patients at approximately 50 sites in the United States.

Travoprost is a synthetic PGA that reduces IOP by enhancing the clearance and drainage of ocular fluid.

We selected travoprost as the active pharmaceutical ingredient for OTX-TP because it:

- is approved by the FDA for the treatment of glaucoma and ocular hypertension;
- has relevant patent protection that expired in December 2014;
- is a highly potent PGA molecule;
- is available from multiple qualified suppliers; and
- has physical properties that are well suited for incorporation within our intracanalicular inserts.

We have designed OTX-TP to deliver therapeutic levels of travoprost for up to three months. We have tested versions of OTX-TP that are capable of local programmed-release over a one-month, a two-month and a three-month period. The retention time of our intracanalicular inserts varies from patient-to-patient due to various physiological and anatomical factors to which the intracanalicular inserts may be subjected. We have conducted a series of non-significant risk, or NSR, investigational device exemption, or IDE, studies with improved product designs and placement procedures with the goal of achieving higher retention rates. We have achieved successive improvements in retention, with as high as a 92% retention rate at day 90 in one of these NSR studies. Our completed pilot studies evaluated one-month and two-month versions of OTX-TP. In our Phase 2a clinical trial, we evaluated two-month and three-month versions of OTX-TP. In our Phase 2b clinical trial, we evaluated an improved three-month version of OTX-TP. In our pilot studies, the OTX-TP inserts we evaluated were violet to provide a visual assessment of insert position. In our subsequent Phase 2 clinical trials, we switched to a fluorescent yellow color to improve visibility and are using this same fluorescent marker in our Phase 2b clinical trial.

In addition to the PEG-based hydrogel, OTX-TP contains bioresorbable microparticles which contain encapsulated travoprost. We designed OTX-TP to deliver travoprost at therapeutic levels for the duration of therapy as the microparticles degrade. We provide OTX-TP in a sterile, single use package without any added preservatives.

## **Overview of OTX-TP Clinical Development**

We are conducting clinical development of OTX-TP for glaucoma and ocular hypertension. Because OTX-TP incorporates an active pharmaceutical ingredient already approved by the FDA for the treatment of glaucoma and ocular hypertension, we did not need to conduct Phase 1 clinical trials for this product candidate. However, we did conduct two pilot studies to assess safety and to obtain initial efficacy data. The following summarizes our clinical development to date for OTX-TP.

- In 2012, we conducted two pilot studies evaluating the safety and efficacy of two versions of OTX-TP for the treatment of glaucoma and ocular hypertension over a 30 to 60 day period.
- In 2014, we completed a Phase 2a clinical trial of two versions of OTX-TP for the treatment of glaucoma and ocular hypertension to evaluate reduction in IOP over a 60 to 90 day period. This completed trial provided important information regarding the effects in patients of the drug delivery rates for our inserts that informed the design of the OTX-TP insert that we used in our Phase 2b clinical trial for this indication.
- In the November 2014, we initiated a Phase 2b clinical trial of OTX-TP for the treatment of glaucoma and ocular hypertension to evaluate reduction in IOP over a 60 to 90 day period. We reported topline efficacy results from this trial in October 2015. There were no hyperemia-related adverse events noted in any of the patients treated with OTX-TP. Further, there have been no serious adverse events observed to date in the Phase 2b trial. Adverse events noted include punctal stenosis, punctal trauma and canaliculitis.
- We have conducted NSR studies on additional modified intracanalicular insert design. We met with the FDA in the second quarter of 2016 to discuss alternative Phase 3 clinical trial designs and to formulate our plans for our Phase 3 program. Based on feedback from this meeting with the FDA, we initiated the first of two planned Phase 3 clinical trials in September 2016.

The trial design for the two Phase 3 clinical trials includes an OTX-TP treatment arm and a placebo-controlled comparator arm using a non-drug-eluting insert. No timolol comparator or validation arm will be required in the study design and no eye drops, placebo or active, are being administered in either arm. We expect that the FDA will require that OTX-TP show both a statistically superior reduction of IOP, when compared to the placebo, as a primary efficacy endpoint, and a clinically meaningful reduction of IOP in the absolute. The primary efficacy endpoint will be evaluated at 2 weeks, 6 weeks and 12 weeks at 8am, 10am and 4pm at each of the three timepoints.

### ***Clinical Trials for Glaucoma and Ocular Hypertension***

#### ***Completed Singapore Pilot Study***

In 2012, we completed a prospective, single arm, open-label pilot study evaluating the initial safety and efficacy of the one-month version of OTX-TP for the treatment of glaucoma and ocular hypertension. We conducted this trial in 17 patients, and in 26 eyes, at two sites in Singapore.

We enrolled patients in this trial who were at least 21 years of age with a documented diagnosis of ocular hypertension or open-angle glaucoma, baseline IOP within a specified range and a specified minimum level of visual acuity in each eye. The trial protocol provided that if the participant's IOP was high despite treatment with OTX-TP, rescue medication would be made available to the patient. For patients who were currently under treatment for ocular hypertension or glaucoma, we required a drug washout period for these medications between screening and first visit.

We evaluated patients at days 3, 10, 20 and 30 following insertion of the insert and made the following assessments:

- mean IOP at 8:00 a.m. at each evaluation date as measured in millimeters of mercury, or mmHg;
- mean IOP at 10:00 a.m. and 4:00 p.m. at days 10, 20 and 30;
- change in mean IOP from baseline at each time point measured; and

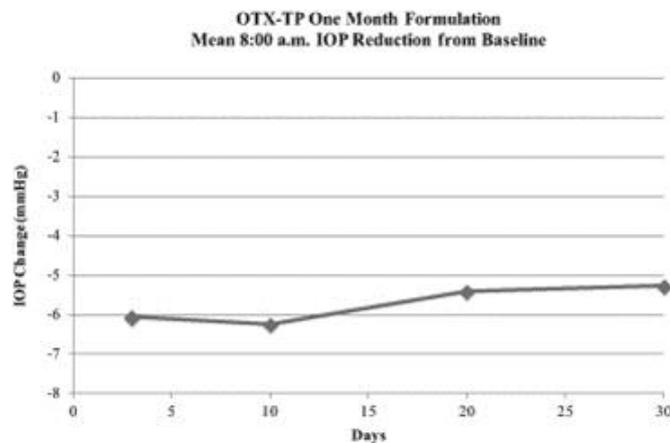
- retention of the insert in the canaliculus at days 10, 20 and 30.

We assessed IOP at multiple time points on each evaluation date because IOP naturally varies over the course of the day.

For patients who are affected bilaterally, if both eyes met all eligibility criteria, both eyes were treated, but only the eye with the higher mean IOP at baseline was included in the efficacy analysis.

**Efficacy:** On day 10, 100% of the inserts were visualized, on day 20, 88% of the inserts were visualized, and on day 30, 79% of the inserts were visualized.

We observed a clinically meaningful reduction in mean IOP over the 30 day trial period. For eyes that retained the insert, from a mean baseline IOP of 27.2 mmHg, the mean IOP during treatment was maintained at or below 22 mmHg at each evaluation date and time point. The mean reduction in IOP from baseline ranged from 5.3 mmHg (20%) to 8.2 mmHg (30%) across all evaluation dates and time points. In studies conducted by third parties, a sustained 5.0 mmHg reduction in IOP reduced risk of disease progression by approximately 50%. The results for change in mean IOP from baseline at 8:00 a.m. on each evaluation date are set forth in the graph below.



**Safety:** In this trial, there were no serious adverse events or unanticipated adverse events. There was only one adverse event, bilateral epiphora, or excess tearing of both eyes, which was transient in nature and completely resolved after insert removal. There were no significant changes in hyperemia scores from baseline through day 30. There were no notable observations of clinical relevance among the slit lamp biomicroscopy assessments.

#### *Completed South Africa Pilot Study*

In 2012, we completed a prospective, single arm, open-label pilot study evaluating the initial safety and efficacy of the two-month version of OTX-TP for the treatment of glaucoma and ocular hypertension. We conducted this trial in 20 patients, and in 36 eyes, at two sites in South Africa.

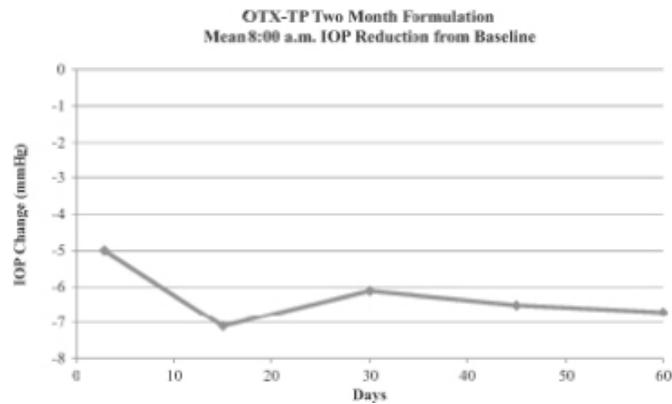
Enrollment criteria were comparable to our Phase 1 Singapore trial described above, except that the minimum patient age was 18.

We evaluated patients at days 3, 15, 30, 45 and 60 following insertion of the insert and made the same assessments with respect to mean IOP, change in mean IOP from baseline and retention of the insert in the canaliculus at each evaluation date following day 3 as in our Phase 1 Singapore trial described above.

**Efficacy:** On day 15, 97% of the inserts were retained, on day 30, 92% of the inserts were visualized, on day 45, 78% of the inserts were retained, and on day 60, 59% of the inserts were retained. Because of the limitations of the visualization of the violet color through pigmented eyelids, it is possible that intracanalicular inserts identified as not being retained were in fact retained but not visible, particularly given the sustained reduction in IOP through day 60

described below. We have since eliminated the violet colorant in favor of a fluorescent PEG hydrogel, resulting in greatly improved visualization.

We observed a clinically meaningful reduction in mean IOP over the 60 day trial period. For eyes that retained the insert, from a mean baseline IOP of 28.7 mmHg, the mean IOP during treatment was maintained at or below 22.0 mmHg beginning on day 15 and at all subsequent evaluation dates. The mean reduction in IOP from baseline ranged from 5.0 mmHg (18%) to 7.1 mmHg (25%) across all evaluation dates and time points. The results for change in mean IOP from baseline at 8:00 a.m. on each evaluation date are set forth in the graph below for patients who retained the insert on such date.



There were only two cases in which IOP remained high even though the insert was confirmed to be present. In each of these cases, the investigator prescribed rescue medication at the end of the visit. It is possible that this elevated IOP was the result of the participants not responding to travoprost.

**Safety:** In this trial, there were no serious adverse events or unanticipated adverse events. The most common adverse event was inflammatory reaction, which was noted in three patients. All adverse events were transient in nature and completely resolved by the end of the trial. There were no significant changes in hyperemia scores from baseline through day 60. There were no notable observations of clinical relevance among the slit lamp biomicroscopy assessments.

#### *Completed South Africa Phase 2a Clinical Trial*

In May 2014, we completed a prospective, randomized, multi-arm, active-controlled, multicenter, double masked Phase 2 clinical trial evaluating the safety and efficacy of two versions of OTX-TP for the treatment of glaucoma and ocular hypertension. The OTX-TPa version was intended to release travoprost over a two-month period, and the OTX-TPb version was intended to release travoprost at a slower rate over a three-month period. Based on *in vitro* testing, the OTX-TPa version had an average daily drug delivery rate of 3.5 micrograms per day and the OTX-TPb version had an average daily drug delivery rate of 2.8 micrograms per day. We conducted this trial in 41 patients at four sites in South Africa. In this trial, we randomized 11 patients for treatment with OTX-TPa and placebo eye drops, 17 patients for treatment with OTX-TPb and placebo eye drops and 13 patients for treatment with a placebo vehicle control intracanalicular insert without active drug and timolol eye drops. One patient randomized into the timolol group was excluded from the trial because the investigator was unable to insert the insert. We randomized more patients in the OTX-TPb group than in the OTX-TPa group because we ceased enrolling patients in the OTX-TPa group during the trial based on an amendment to our trial protocol intended to facilitate the completion of the trial and to allow us to evaluate a larger number of patients being treated with a three-month version of the insert. Timolol is the most commonly prescribed non-PGA drug for the treatment of glaucoma and has been used as a comparator drug in pivotal clinical trials for other approval glaucoma products.

The primary efficacy endpoints in this trial are differences between treatment groups in:

- mean change in IOP from baseline on each evaluation date and at each time point;

- mean percent change in IOP from baseline on each evaluation date and at each time point; and
- mean IOP on each evaluation date and at each time point.

We designed our Phase 2a clinical trial to assess clinically meaningful response to treatment, and did not power the trial to measure any efficacy endpoints with statistical significance. We also evaluated retention of the insert as a secondary endpoint.

We enrolled patients in this trial who were at least 18 years of age with a documented diagnosis of ocular hypertension or open-angle glaucoma, baseline IOP within a specified range and a specified minimum level of visual acuity in each eye. We excluded patients from this trial if, among other reasons, they had a history of inadequate response to treatment with prostaglandins or beta-blockers. For patients who were currently under treatment for ocular hypertension or glaucoma, we required a drug washout period for these medications between screening and first visit.

We evaluated patients at days 3, 15, 30, 45, 60, 75 and 90 following insertion of the insert and made the following assessments:

- mean IOP at 8:00 a.m. at each evaluation date;
- mean IOP at 12:00 p.m. and 4:00 p.m. at days 30, 60 and 90;
- change in mean IOP from baseline at each time point measured; and
- retention of the insert in the canaliculus at each evaluation date.

For patients who are affected bilaterally, if both eyes met all eligibility criteria, both eyes were treated, but only the eye with the higher mean IOP at baseline was included in the primary efficacy analysis.

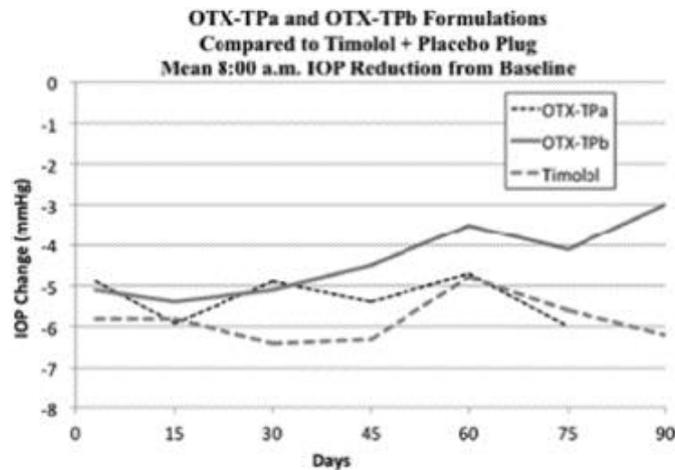
We evaluated safety in all patients at each study visit with an assessment of general eye conditions, including visual acuity, along with any adverse events.

**Efficacy:** In the timolol group, for eyes that retained the insert, from a mean baseline IOP of 26.1 mmHg, the mean IOP during treatment was maintained at or below 21.4 mmHg beginning on day 15 and at all subsequent evaluation dates and time points. The mean reduction in IOP from baseline ranged from 3.2 mmHg (13%) to 6.4 mmHg (25%) across all evaluation dates and time points through day 75.

In the OTX-TPa group, for eyes that retained the insert, from a mean baseline IOP of 25.8 mmHg, the mean IOP during treatment was maintained at or below 21.0 mmHg beginning on day 15 and at all subsequent evaluation dates and time points through day 75. The OTX-TPa formulation, originally intended to deliver drug over a two-month period, exceeded our expectations, delivering drug for 75 days. The mean reduction in IOP from baseline ranged from 3.2 mmHg (14%) to 6.0 mmHg (24%) across all evaluation dates and time points through day 75.

In OTX-TPb group, for eyes that retained the insert, from a mean baseline IOP of 26.4 mmHg, the mean IOP during treatment was maintained at or below 22.2 mmHg beginning on day 15 and at all subsequent evaluation dates and time points. The mean reduction in IOP from baseline ranged from 2.0 mmHg (9%) to 5.4 mmHg (20%) across all evaluation dates and time points.

The results for change in mean IOP for patients in the OTX-TPa group, for patients in the OTX-TPb group and for patients in the timolol group from baseline at 8:00 a.m. on each applicable evaluation date are set forth in the graph below, in each case for patients who retained the insert on such date. We believe that the lower average daily drug delivery rate in the OTX-TPb group may have resulted in less reduction of mean IOP in this group as compared to the OTX-TPa group. As discussed below, we evaluated an improved three-month version of OTX-TP in our Phase 2b clinical trial.



**Safety:** In this trial, there were no serious adverse events. The most common adverse event was inflammatory reaction, which was noted in five patients. All adverse events were transient in nature and resolved by the end of the trial. There were no significant changes in hyperemia scores from baseline through day 90. There were no notable observations of clinical relevance among the slit lamp biomicroscopy assessments.

#### *Completed U.S. Phase 2b Clinical Trial*

In November 2014, we initiated a prospective, randomized, parallel-arm, active-controlled, multicenter, double-masked Phase 2b clinical trial to evaluate the safety and efficacy of OTX-TP for the treatment of glaucoma and ocular hypertension after submitting an IND to the FDA for this indication. We treated 73 patients at 11 sites in the United States pursuant to our effective IND. We randomized patients in a 1:1 ratio to receive either OTX-TP and placebo eye drops or a placebo vehicle control intracanalicular insert without active drug and eye drops containing timolol. Patients were instructed to use the placebo drops or timolol drops twice daily for the duration of the trial. Based on the results of our completed Phase 2a clinical trial, we designed the OTX-TP insert for use in our Phase 2b clinical trial to deliver drug over a 90 day period at the same daily rate as the OTX-TPa 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. We previously evaluated in our Phase 1 clinical trial of OTX-MP in patients following cataract surgery an insert of similar size to the insert we are using in our Phase 2b clinical trial. These structural changes were previously evaluated in NSR studies that we describe below.

The primary efficacy endpoint in this trial was the difference between treatment groups in the mean change in IOP from baseline at day 60 following insertion of the intracanalicular insert, calculated by averaging the change from baseline across the three time points at the assessment date, which is known as diurnal IOP. The secondary efficacy endpoints in this trial were the difference between treatment groups in the mean change from baseline in average diurnal IOP at day 90, the difference between treatment groups in the mean change from baseline in IOP at each individual time point at day 60 and day 90, the difference between treatment groups in the mean change in average diurnal IOP and IOP at each individual time point at day 60 and day 90, and the difference between treatment groups in the mean percent change from baseline in average diurnal IOP and IOP at each individual time point at day 60 and 90. We designed our Phase 2b clinical trial to assess clinically meaningful response to treatment, and did not power the trial to measure any efficacy endpoints with statistical significance.

We enrolled patients in this trial who are at least 18 years of age with a documented diagnosis of ocular hypertension or open-angle glaucoma, baseline IOP within a specified range and a specified minimum level of visual acuity in each eye. We excluded patients from this trial if, among other reasons, they had a history of inadequate response to treatment with prostaglandins or beta-blockers. For patients under treatment for ocular hypertension or glaucoma, we required a drug washout period for these medications between screening and first visit. We also evaluated the effect of a four week versus a five week washout duration on the change in 8:00 a.m. IOP in both groups.

We evaluated patients at days 3, 15, 30, 45, 60, 75 and 90 (with insertion of the insert on day 1) and made the following assessments:

- mean IOP and change in mean IOP from baseline at 8:00 a.m. at days 3, 15, 45 and 75; and
- mean IOP and change in mean IOP from baseline at 8:00 a.m., 12:00 p.m. and 4:00 p.m. at days 30, 60 and 90.

We also collected data on intracanalicular insert presence along with visualization of the insert by both the study patient and the investigator. The patients were instructed to assess insert presence on a daily basis and report the absence of an insert immediately. This data has provided a method for us to assess the accuracy of patient self-examination for insert presence, and we expect that this will maximize the consistency of dosing.

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

### **Efficacy:**

In this trial, the mean change from baseline IOP at 8:00 a.m. on day 30, 60, and 90 in the OTX-TP group was a decrease of 4.5, 4.7, and 5.1 mm Hg, respectively.

In this trial, on day 60, the OTX-TP group experienced a mean diurnal IOP lowering effect of 3.3 mmHg compared to baseline, versus mean diurnal IOP lowering of 5.9 mmHg compared to baseline for the timolol group. On day 90, the OTX-TP group experienced a mean diurnal IOP lowering effect of 3.6 mmHg compared to baseline, versus mean diurnal IOP lowering of 6.3 mmHg compared to baseline for the timolol group.

On day 60, the OTX-TP group experienced a mean IOP lowering effect compared to baseline of 4.7 mmHg at 8:00 a.m., 2.3 mmHg at 12:00 p.m. and 2.8 mmHg at 4:00 p.m., versus mean IOP lowering compared to baseline of 6.4 mmHg at 8:00 a.m., 6.1 mmHg at 12:00 p.m. and 5.6 mmHg at 4:00 p.m. for the timolol group. On day 90, the OTX-TP group experienced a mean IOP lowering effect compared to baseline of 5.1 mmHg at 8:00 a.m., 2.5 mmHg at 12:00 p.m. and 3.0 mmHg at 4:00 p.m., versus a mean IOP lowering effect compared to baseline of 7.2 mmHg at 8:00 a.m., 6.1 mmHg at 12:00 p.m. and 5.5 mmHg at 4:00 p.m. for the timolol group.

The mean IOP in the OTX-TP treatment group on day 60 was 21.73 mmHG at 8:00 a.m., 22.27 mmHg at 12:00 p.m. and 21.42 mmHg at 4:00 p.m. In the timolol group, the mean IOP on day 60 was 20.74 mmHg at 8:00 a.m., 19.05 mmHg at 12:00 p.m. and 18.85 mmHg at 4:00 p.m. The mean IOP in the OTX-TP treatment group on day 90 was 21.33 mmHg at 8:00 a.m., 22.09 mmHg at 12:00 p.m. and 21.18 mmHg at 4:00 p.m. In the timolol group, the mean IOP on day 90 was 19.87 mmHg at 8:00 a.m., 19.08 mmHg at 12:00 p.m. and 18.95 mmHg at 4:00 p.m.

The mean diurnal IOP in the OTX-TP treatment group on day 60 was 21.81 mmHg. The mean diurnal IOP in the timolol treatment group on day 60 was 19.54 mmHg.

The mean diurnal IOP in the OTX-TP treatment group on day 90 was 21.53 mmHg. The mean diurnal IOP in the timolol treatment group on day 90 was 19.3 mmHg.

This Phase 2b glaucoma clinical trial was designed to evaluate the non-inferiority of OTX-TP compared to timolol and to inform the further clinical development for OTX-TP. This trial was not powered to show statistical significance between treatment groups. The OTX-TP treatment group included placebo eye drops that may have reduced the efficacy measures for OTX-TP, by washing out drug eluted from the insert from the ocular surface, whereas the timolol group included a placebo insert that may have improved the efficacy of timolol through occlusion of the punctum thereby

prolonging its retention on the ocular surface. Several peer-reviewed medical journals have reported studies in which an additional IOP lowering effect of 1.32 to 1.80 mmHg was observed in patients taking timolol eye drops in combination with a non-drug eluting punctum plug compared to those patients only taking timolol eye drops. These include studies reported in September 2011 in *Clinical and Experimental Optometry*, February 1989 in the *American Journal of Ophthalmology* and August 1996 in *Acta Ophthalmologica Scandinavica*. The expected design for our Phase 3 clinical trials of OTX-TP for the treatment of glaucoma and ocular hypertension is addressed below under “—Regulatory Pathway”.

In the timolol group, the mean IOP at day 30, 60 and 90 at all time points ranged from 18.9 mmHg to 20.7 mmHg. The mean reduction in IOP from baseline at day 30, 60 and 90 at all time points ranged from 5.3 mmHg to 7.3mmHg.

In the OTX-TP group, the mean IOP at day 30, 60 and 90 at all time points ranged from 21.0 mmHg to 22.3 mmHg. The mean reduction in IOP from baseline at day 30, 60 and 90 at all time points ranged from 2.3 mmHg to 5.2 mmHg.

In our completed South Africa Phase 2a clinical trial in which OTX-TP intracanalicular inserts were inserted in 36 eyes in 20 patients with no placebo eye drops used, on day 30 we observed a reduction in IOP of 6.1 mmHg at 8:00 a.m., 5.1 mmHg at 12:00 p.m. and 5.6 mmHg at 4:00 p.m. following insertion of the intracanalicular insert. In this trial, on day 60 we observed a reduction in IOP of 6.7 mmHg at 8:00 a.m., 5.1 mmHg at 12:00 p.m. and 4.3 mmHg at 4:00 p.m. following insertion of the intracanalicular insert. The diurnal averages of the reduction in the IOP were 5.6 mmHg at day 30 and 5.4 mmHg at day 60 in this trial. We believe that the higher IOP reduction observed in this trial may be due in part to the lack of placebo eye drops.

We performed additional post-hoc analyses that were not pre-specified in the trial protocol for the Phase 2b glaucoma clinical trial to provide further insight on the performance of OTX-TP. Although post-hoc analyses performed using an unlocked clinical trial database can result in the introduction of bias, we believe that these analyses provide important information regarding our OTX-TP product candidate and are helpful in determining the study population and inclusion and exclusion criteria for future clinical trials. When we excluded patients on more than one glaucoma medication and used the baseline of five weeks of washout for comparisons of the OTX-TP group and the timolol group, the differences in mean reduction in IOP between the OTX-TP treatment group and the timolol group at the 8:00 a.m. time point on day 30, 60 and 90 narrowed to an average of 1.1 mmHg from an average of 2.2 mmHg based on the pre-specified criteria. These results are shown in the table below:

<b>8:00 am Results for Intraocular Pressure (mmHg)</b>				
	<b>Intent to Treat Population</b>		<b>Post-hoc analysis Baseline of 5 weeks, single drug only</b>	
	<b>OTX-TP</b>	<b>Timolol</b>	<b>OTX-TP</b>	<b>Timolol</b>
Day 30	-4.5	-6.6	-4.9	-6.2
Day 60	-4.7	-6.4	-5.3	-6.2
Day 90	-5.1	-7.3	-5.7	-7.2
<b>Average</b>	-4.8	-7.0	-5.6	-6.7
<b>Difference</b>	-2.2		-1.1	

In this trial, inserts were found to be retained in 91% of patients at day 60, 88% of patients at day 75 and 48% of patients at day 90, reflecting the corresponding absorption and clearance of the inserts with the duration of drug release.

**Safety:** In this trial, there were no serious adverse events. Adverse events noted to date including punctal stenosis, punctal trauma and canaliculitis. The most common adverse event was inflammatory reaction of the lacrimal punctum and/or canaliculus, which was noted in five patients. These adverse events were transient in nature and resolved by the end of the trial. There were no significant changes in hyperemia scores from baseline through day 90 and there were no hyperemia related adverse events. There were no notable observations of clinical relevance among the slit lamp biomicroscopy assessments.

*Non-Significant Risk Retention Studies*

We conduct medical device NSR IDE studies on an ongoing basis for the purpose of refining our intracanalicular insert product and placement procedure. We conduct these NSR studies under FDA IDE regulations, although no

specific FDA approval is required. We are able to conduct NSR studies because intracanalicular inserts without active drug are well established ophthalmic medical devices. The NSR study process allows us to make relatively quick evaluations of our intracanalicular insert design and placement procedure in human subjects.

In a series of completed NSR studies, we have effected compositional and dimensional adjustments to our intracanalicular insert to optimize retention. We have also used these studies to evaluate intracanalicular insert placement, as well as removal and repeat placements and have seen a range of results in NSR studies to date, with the most recent study achieving a retention rate of approximately 85-90% at day 90.

We are using an intracanalicular insert design in our Phase 3 clinical trials of OTX-TP for the treatment of glaucoma and ocular hypertension that is slightly smaller than the plug design used in the Phase 2b clinical trial. We also plan to use an intracanalicular insert design in these trials that has a rapidly dissolvable tip that enables greater ease of insertion of the insert.

We believe that with the current level of retention with our intracanalicular insert design and given the ability of patients to assess the presence of the insert as a result of the fluorescent label, our current product design offers a potentially significant improvement over the current standard of care with patients receiving PGAs. The compliance rate with PGA eye drops has been shown to be only approximately 50% after six months of therapy due to the challenges of administration and side effects including hyperemia, or red eye.

### ***Regulatory Pathway***

Based on feedback following discussions with the FDA in the second quarter of 2016, we are using a protocol design for our Phase 3 clinical trials that focuses on a comparison of the OTX-TP arm against a vehicle placebo arm. We are not required to use placebo drops in this trial or include a timolol reference arm. We will be required to successfully complete two well controlled Phase 3 clinical trials of OTX-TP conducted under an IND to obtain marketing approval from the FDA. We reached our target enrollment of 550 patients at approximately 50 sites in our first Phase 3 clinical trial for an expected exposure duration of three months. A number of patients will be studied for up to 12 months for safety evaluations. Patients will be randomized in a 3:2 ratio to receive either OTX-TP or a placebo vehicle control intracanalicular insert without active drug. There is no timolol comparator or validation arm required in the study design and no eye drops, placebo or active, are being administered in either arm. We expect that the FDA will require that OTX-TP show both a statistically superior reduction of IOP, when compared to the placebo, as a primary efficacy endpoint, and a clinically meaningful reduction of IOP in the absolute. The primary efficacy endpoint will be evaluated at 2, 6 and 12 weeks at 8 a.m., 10 a.m. and 4 p.m. at each of the three timepoints. We initiated the first Phase 3 clinical trial in September 2016 and anticipate topline data in the first half of 2019. We do not intend to initiate the second Phase 3 clinical trial until we receive data from the first Phase 3 clinical trial and discuss the results of this first Phase 3 clinical trial with the FDA.

If we obtain favorable results from these Phase 3 clinical trials, we would plan to submit an NDA to the FDA for marketing approval of OTX-TP for the treatment of glaucoma and ocular hypertension. We expect that we would submit this NDA under Section 505(b)(2) of the FDCA. See “—Governmental Regulation—Section 505(b)(2) NDAs” for additional information.

### ***Intracameral Glaucoma (OTX-TIC) Product Candidate***

We are conducting an open-label, proof-of-concept Phase 1 clinical trial of OTX-TIC that we initiated in the second quarter of 2018 for the treatment of patients with moderate to severe glaucoma and ocular hypertension. OTX-TIC (extended-delivery travoprost) is a bioresorbable hydrogel implant incorporating travoprost that is designed to be an intracameral injection into the anterior chamber of the eye with an initial target duration of drug release of four to six months. Preclinical studies to date have demonstrated clinically meaningful IOP lowering and good pharmacokinetics in the aqueous humor. We initiated a pilot clinical study outside the United States in the third quarter of 2017 to assess safety and obtain initial efficacy data, but did not enroll any patients in this clinical trial and determined to close this trial. We submitted an IND in the first quarter of 2018 and initiated a second Phase 1 trial in the United States in the second quarter of 2018. The study is a prospective, multi-center study to evaluate the safety, efficacy, durability and tolerability of OTX-TIC compared to topical travoprost (eye drops) in patients with open-angle glaucoma or ocular

hypertension. The first patient in this trial has been treated for nine months from dosing. We expect to present initial results at the Association of Research and Vision of Ophthalmology meeting in April 2019.

### **Intravitreal Implants for the Treatment of Back-of-the-Eye Diseases**

We are engaged in a preclinical development program of our sustained-release hydrogel administered via intravitreal injection to address the large and growing markets for diseases and conditions of the back of the eye. Our current 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 both small and large molecule 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 have demonstrated a sustained pharmacodynamic effect *in vivo* of up to six months with a small molecule tyrosine kinase inhibitor (TKI). The two strategies being pursued are as follows:

- We are evaluating an intravitreal implant, in collaboration with Regeneron, consisting of a PEG-based hydrogel matrix containing embedded micronized particles of aflibercept. Aflibercept is marketed by Regeneron under the brand name Eylea. We refer to the formulation we are developing with Regeneron as OTX-IVT. We designed the injection to be delivered to the vitreous chamber of the eye using a fine gauge needle. We entered into a strategic collaboration with Regeneron in October 2016 for the development and commercialization of protein-based anti-VEGF drugs, with the initial product candidate incorporating the drug aflibercept into our hydrogel.
- We have selected the TKI, referred to as OTX-TKI, and advanced into an initial human clinical trial and dosed our first patient in Australia in February 2019. We have conducted preclinical work on this compound and have achieved local programmed-release and pharmacodynamic effect *in vivo* for six months. We believe this class of drugs 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, these drugs 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. 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.

We are conducting these small and large molecule local programmed-release programs in parallel.

#### *In Vitro and Preclinical results*

To date, in *in vitro* tests and preclinical studies, we have been able to incorporate antibody anti-VEGF drugs within our hydrogels, and our collaborators have been testing release rates and the integrity and activity of their compounds. We have achieved *in vitro* release over a four to six month duration. The released proteins have been stable, with no chemical or functional changes observed.

Our hydrogel implants have shown initial tolerability and acceptable pharmacokinetics. We conducted an *in vivo* study to measure ocular tissue concentrations of bevacizumab after injection with and without our sustained-release hydrogel. The injection of a bevacizumab formulation without our hydrogel resulted in a first-order rate of drug clearance, as expected. In addition, bevacizumab concentrations decreased in the ocular tissues with distance from the intravitreal injection site. The injection of our hydrogel implant containing bevacizumab showed the same decrease of tissue concentration of bevacizumab in successively distant tissues. However, the injection of our hydrogel implant containing bevacizumab resulted in a sustained level of drug over the course of the 30 day study. Further, after injection of our hydrogel implant containing bevacizumab, we observed levels of drug in ocular tissues over the course of the study that were consistent with our *in vitro* release data. After two weeks, the drug concentrations of the implant exceeded those of bevacizumab injected without our hydrogel. More recently, we have conducted a pharmacodynamic study in a rabbit model, achieving activity against an intravitreal VEGF challenge injection after study duration of four months, compared to less than six weeks for a 1.25 mg (human dose) bevacizumab intravitreal injection. Tolerability of

bevacizumab-loaded implants in rabbit eyes has been demonstrated through four months. In addition, there were no anti-drug antibodies detected in these rabbits, even though bevacizumab is a recombinant humanized monoclonal antibody and therefore might be expected to elicit an immune response in rabbits. This early feasibility study has provided us with initial encouraging data for our sustained-release hydrogel implant with bevacizumab and its potential capability of delivering active drug to ocular tissues in a local programmed-release fashion and informs the additional preclinical activities we plan to pursue. Although these results have been encouraging, we will need to further optimize our hydrogels for aflibercept in our collaboration with Regeneron. We believe we have demonstrated initial feasibility sufficient to support the continuing preclinical development of this program and, if we obtain additional favorable preclinical results, advancement into Phase 1 clinical trials.

We have conducted *in vivo* pharmacokinetic and pharmacodynamic studies with hydrogels loaded with a small molecule anti-angiogenic TKI compound injected intravitreally. Pharmacokinetic data showed retinal tissue drug concentrations in excess of 3,000 times published IC50 after six months and pharmacodynamic results show sustained efficacy for six months.

We also continue to conduct our own internal preclinical development program using TKIs. We also believe there are other opportunities for targets beyond VEGF-related targets to utilize our hydrogel for back-of-the-eye diseases, and we may pursue opportunities through internal research or in partnership with pharmaceutical companies.

## **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.

### ***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.

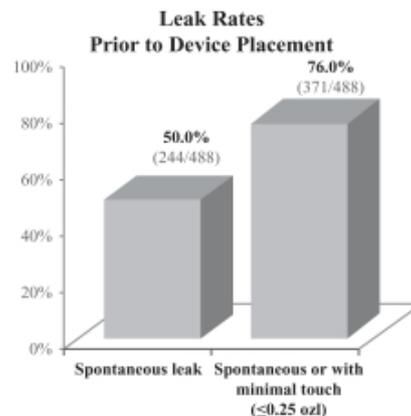
*Pivotal Clinical Trial*

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.

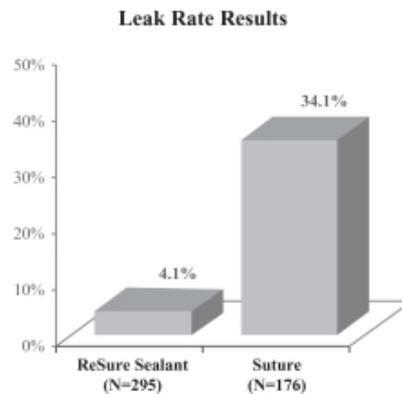
The primary efficacy endpoint was non-inferiority of ReSure Sealant to sutures for preventing incision leakage from clear corneal incisions within the first seven days following cataract surgery. A non-inferiority determination requires that the test product is not worse than the comparator by more than 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 included two post-approval studies as a condition of the PMA application approval.

The first post-approval study, identified as the Clinical PAS, is to confirm that ReSure Sealant can be used safely by physicians in a standard cataract surgery practice and to confirm the incidence in eyes treated with ReSure Sealant of the most prevalent adverse ocular events identified in our pivotal study of ReSure Sealant in eyes treated with ReSure Sealant. The FDA has approved the protocol for the Clinical PAS, and we initiated enrollment in December 2014. Enrollment was completed in December 2015 with 626 patients in 22 sites. We submitted the final study report to the FDA in June 2016, and the FDA has subsequently 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. We initiated enrollment in this study in December 2016 and submitted our first progress report to FDA in January 2017. The Device Exposure Registry Study is required to include at least 4,857 patients. 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. We have provided regular periodic reports to the FDA on the progress of this post-approval study.

We received a warning letter from the FDA in October 2018 relating to our compliance with data collection and information reporting obligations in the Device Exposure Registry Study. The FDA warning letter refers to a lack of progress with the enrollment and related data collection and information reporting obligations for a required post-approval trial. In November 2018, we appealed this warning letter. On December 26, 2018, the FDA rejected our appeal. 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. We continue to work with FDA to find a path to evaluate the incidence of endophthalmitis in patients receiving ReSure. ReSure Sealant currently remains commercially available in the United States, though there is no sales support provided to the product at this time.

### *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.

### **Commercial Strategy**

Our goals for ReSure Sealant are to provide a novel means of definitive wound closure in situations in which the surgeon would otherwise use sutures and to increase the number of procedures in which surgeons close the wound following cataract surgery, instead of leaving the wound to self-seal. 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. As a result, the market opportunity for a surgical sealant following cataract surgery may be modest. However, we believe ReSure Sealant offers important benefits over sutures, including superior wound closure, a better safety profile and less follow-up. While ReSure Sealant remains commercially available in the United States, there is no current sales support provided to the product at this time. We would anticipate that ReSure will be supported by the sales force being put in place to launch DEXTENZA once commercialization begins.

### **Sales, Marketing and Distribution**

We commercially launched ReSure Sealant in the United States in February 2014. We initially sold ReSure Sealant through a network of independent distributors across the United States. While ReSure Sealant remains commercially available in the United States, there is no sales support provided to the product at this time. However, with the approval of DEXTENZA, we expect to be able to sell ReSure Sealant with DEXTENZA with any sales force we establish for DEXTENZA. Although we do not actively promote ReSure Sealant in terms of territory sales representatives, we continue to maintain a promotional presence for ReSure Sealant in the ophthalmic marketplace through podium presence at major conventions, such as the American Society of Cataract and Refractive Surgery and the American Academy of Ophthalmology.

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.

With the approval of DEXTENZA in November of 2018, we are building a highly targeted, key account sales force that will focus on the ambulatory surgical centers responsible for the largest volumes of cataract surgery. In support of the commercial launch of DEXTENZA, we submitted an application for a C-code for transitional payment status upon the approval of the product and expect to ascertain a C-code by the end of the second quarter of 2019 to

enable first commercial sales in the third quarter of 2019. We also submitted a sNDA in January 2019 in order to expand the DEXTENZA label to include post-surgical ocular inflammation.

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. These may include independent distributors, pharmaceutical companies or our own direct sales organization.

We have entered into a strategic collaboration with Regeneron for the commercialization of our intravitreal implant for the delivery of protein-based anti-VEGF drugs for the treatment of back-of-the-eye diseases, including wet AMD, which is currently in a preclinical stage of development.

## **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 relocated our corporate headquarters to the new leased premises in June 2017 and 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 have a one-time option to terminate the manufacturing space lease on July 2021, upon the delivery to the landlord on or before July 2020 a termination notice and the payment to the landlord of a termination fee.

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 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 have in-licensed all of our patent rights 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

March 1, 2019, we have licensed from Incept a total of 20 U.S. patents, 8 U.S. patent applications and foreign counterparts of some of these patents and patent applications. Our license from Incept includes the following:

*Intracanalicular Insert and Intracameral Implant Product Candidates*

We have six U.S. patents that cover our intracanalicular insert and intracameral implant product candidates. Two patents which have issued in the U.S. and Japan, and are pending in the European Union and elsewhere, which are expected to expire in 2030 and cover compositions and methods of use of intracanalicular inserts. These patents are licensed exclusively to us in the field of ophthalmology. Two U.S. patents which are expected to expire in 2020 and cover the hydrogel composition of the intracanalicular inserts and methods of making and using hydrogel implants. These patents are licensed exclusively to us in the field of ophthalmology. A U.S. patent which is expected to expire in 2024 that covers the process of making the hydrogel composition of OTX-TP and OTX-MP and are non-exclusively licensed to us. A pending U.S. patent application that covers the hydrogel composition of DEXTENZA that, if granted, is expected to expire in 2027.

*ReSure Sealant*

We have two U.S. patents that cover ReSure Sealant. A U.S. patent which is expected to expire in 2024 and which covers the process of making and using hydrogel compositions. A U.S. patent which is expected to expire in 2032 and which covers certain features of the ReSure Sealant package. Outside of the United States, we have exclusively licensed only one patent in Canada that is expected to expire in 2019 and is directed to a medical kit for use with ReSure Sealant.

*Intravitreal Injection*

We have two U.S. patents that cover intravitreal injection product candidates. A U.S. patent that is expected to expire in 2027 and patent applications which are pending in the European Union covering certain drug-release features of the hydrogel implant in combination with its hydrogel composition and other proprietary technology relating to intravitreal injections, and which, if granted, are expected to expire in 2027. A granted U.S. patent which is expected to expire in 2033 and pending patent applications in the European Union, Japan, U.S. and certain other jurisdictions covering the process of making the hydrogel implant with its drug release features and the resultant compositions and other proprietary technology that, if granted are expected to expire in 2032.

A pending patent application in the U.S. and a PCT application that is expected to serve as the basis for filings in multiple countries outside of the United States directed to a drug delivery vehicle and other proprietary technology that, if granted, are expected to expire in 2036.

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.

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 all of the patent rights and a significant portion of 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 current Executive Chairman of the Board of Directors, is a general partner of Incept.

On September 13, 2018, or the Effective Date, the Company 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 the Company's intellectual property license and modify future intellectual property ownership and other rights thereunder.

*License Rights; Ownership of Intellectual Property.* The parties have agreed to expand the field of use of the exclusive, worldwide, perpetual, irrevocable license held by the Company 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. The parties 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.

The Company will solely own, without a license to Incept, all intellectual property rights conceived solely by one or more individuals from the 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 Company (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.* The Company and any of its 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 Company or its 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 the Company or its 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 the Company or its 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 the Company 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 the Company. Additionally, at its sole discretion, Incept may require, as a condition of any sublicense by the Company 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 the Company 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 the Company 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, the Company would assume control of the prosecution of patents and patent applications included in or arising under the Shape-Changing IP. The Company has 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. The Company has 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. The Company is 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 the Company 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.

### ***Regeneron Collaboration***

In October 2016, we entered into the Collaboration Agreement with Regeneron for the development and commercialization of products using the Company's sustained-release hydrogel in combination with Regeneron's large molecule VEGF-targeting compounds to address conditions of the eye.

Under the terms of the Collaboration Agreement, we and Regeneron have 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. We have granted Regeneron the Option to enter into an exclusive, worldwide license, with the right to sublicense, under our intellectual property to develop and commercialize the Licensed Products. The Option is exclusive until 12 months after Regeneron has received a product candidate in accordance with a collaboration plan, subject to certain conditions, and non-exclusive for an additional six months following the end of the exclusive period. The field of this license is limited to 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 does not cover the development of any products that deliver small molecule drugs, including TKIs, or deliver large molecule drugs other than those that target certain specified VEGF proteins or their receptors. Under the terms of the Collaboration Agreement, Regeneron is responsible for funding an initial preclinical tolerability study, which it initiated in early 2018.

If the Option is exercised, Regeneron is to use commercially reasonable efforts to conduct further preclinical development and an initial clinical trial under a collaboration plan. We are 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 million, which cap may be increased by up to \$5 million under certain circumstances. We are also responsible for paying our own costs associated with the activities conducted by us under the collaboration plan. If Regeneron elects to proceed with further development following the completion of the collaboration plan, it will be solely responsible for conducting and funding, and is to use commercially reasonable efforts with respect to, further development and commercialization of product candidates.

Under the terms of the Collaboration Agreement, Regeneron has agreed to pay us \$10 million upon exercise of the Option. We are also eligible to receive up to \$145 million per Licensed Product upon the achievement of specified

development and regulatory milestones, \$100 million per Licensed Product upon first commercial sale of such Licensed Product and up to \$50 million based on the achievement of specified sales milestones for all 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 Licensed Products, which royalties are subject to potential reductions in certain circumstances, subject to a minimum royalty.

If Regeneron has not exercised the Option during the designated option period, the Collaboration Agreement will expire. If Regeneron exercises the Option, the 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. Following expiration, Regeneron will have a fully paid-up, non-exclusive license to continue to develop and commercialize Licensed Products. The Collaboration Agreement may be terminated by Regeneron at any time after exercise of the Option upon 60 days' 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.

In December 2017, we delivered to Regeneron the final formulation for Regeneron's initial preclinical tolerability study. Regeneron initiated this study in early 2018 and is responsible for its funding. While we await a decision from Regeneron regarding the Option, we are not actively pursuing further formulation development or other preclinical testing under the Collaboration Agreement.

## **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, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Our potential competitors include large pharmaceutical and biotechnology companies, and specialty pharmaceutical and generic drug companies. 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.

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 any products that we may develop. 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. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products.

Our 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 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, seek to encourage the use of generic products. Given that we are developing products based on FDA-approved therapeutic agents, our 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.

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 intracanalicular insert product candidates, as set forth below.

#### ***Competitors of DEXTENZA***

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. Icon Biosciences Inc. was subsequently bought by pSvidia Corporation in March 2018 and, at the same time, the new entity was renamed Eyepoint Pharmaceuticals, Inc., or Eyepoint. In January 2019, Eyepoint announced that DEXYCU's J-Code became effective and Eyepoint expected to launch DEXYCU commercially in the first quarter of 2019.

#### ***Competitors of OTX-TP***

Allergan, Inc. is conducting Phase 3 clinical development and plans to submit an NDA for Bimatoprost Sustained-Release, a biodegradable intraocular implant consisting of a PGA and a biodegradable polymer matrix for the treatment intended to reduce IOP in patients with glaucoma. 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. 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 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 is not currently available 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.

#### ***Competitors of our Intravitreal 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 and off-label use of the cancer therapy Avastin. Multiple companies are exploring ways to deliver anti-VEGF products in a sustained-release fashion, although all are in early stages of development.

## 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. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an 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 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. Similar requirements for posting clinical trial information are present in the European Union (EudraCT) website: <https://eudract.ema.europa.eu/> and other countries, as well.

#### *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.

On December 13, 2016, the 21st Century Cures Act established (and the 2017 Food and Drug Administration Reauthorization Act later amended) a requirement that sponsors of one or more investigational drugs for the treatment of a serious disease(s) or condition(s) make publicly available their policy for evaluating and responding to requests for expanded access for individual patients. Although these requirements were rolled out over time, they have now come into full effect. This provision requires drug and biologic companies 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 or the sponsor or the data monitoring committee may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. 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.

#### *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 2019 is \$2,588,478 for an application requiring clinical data. The sponsor of an approved application is also subject to an annual program fee, which for fiscal year 2019 is \$309,915. 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. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter 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. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, 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.

The FDA must establish a priority review track for certain generic drugs, requiring the FDA to review a drug application within eight months for a drug that has three or fewer approved drugs listed in the Orange Book and is no longer protected by any patent or regulatory exclusivities, or is on the FDA's drug shortage list. The FDA is also

authorized to expedite review of “competitor generic therapies” or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

#### *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, 2019, the FDA has approved 17 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 Studies and Exclusivity*

Under the Pediatric Research Equity Act of 2003, an NDA 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 Administration Safety and Innovation Act, or 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. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

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 FDASIA. In addition, products that have received orphan designation are exempt from the requirements of the Pediatric Research Equity Act.

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, require 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 2018, the standard fee is \$310,764.

#### *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 Drug 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, which is set to replace the current Clinical Trials Directive. The new Clinical Trial Regulation was published on June 16, 2014 but is not expected to apply until sometime in 2019. The new Clinical Trials Regulation will be directly applicable to and binding in all 28 EU Member States without the need for any national implementing legislation, and will become applicable no earlier than 28 May 2016. 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 Clinical Trials Regulation also aims to streamline and simplify the rules on safety reporting for clinical trials.

#### *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 with 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 EU, medical devices must comply with the Essential Requirements in Annex I to the 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. Actual implementation of these directives, however, may vary on a country-by-country basis.

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 its 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. In September 2012, the European Commission adopted a proposal for a regulation which, if adopted, will change the way that most medical devices are regulated in the European Union, and may subject products to additional requirements.

#### *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 European Union (commonly referred to as Brexit). Thereafter, on March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The withdrawal of the United Kingdom from the European Union will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the United Kingdom provides a notice of withdrawal pursuant to the EU Treaty. 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 European Union directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the United Kingdom.

The United Kingdom has a period of a maximum of two years from the date of its formal notification to negotiate the terms of its withdrawal from, and future relationship with, the European Union. If no formal withdrawal agreement is reached between the United Kingdom and the European Union, then it is expected the United Kingdom's membership of the European Union will automatically terminate two years after the submission of the notification of the United Kingdom's intention to withdraw from the European Union. Discussions between the United Kingdom and the European Union focused on finalizing withdrawal issues and transition agreements are ongoing. However, limited progress to date in these negotiations and ongoing uncertainty within the UK Government and Parliament sustains the possibility of the United Kingdom leaving the European Union on March 29, 2019 without a withdrawal agreement and associated transition period in place, which is likely to cause significant market and economic disruption.

#### *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 & 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, or C-code, for DEXTENZA on November 30, 2018 from the Centers for Medicare and Medicaid Services, or CMS, and expect pricing for DEXTENZA while in pass-through status to be approximately \$540 per surgery. We expect pass-through would remain in effect for up to three years depending on when we apply for and receive this reimbursement code. We submitted an application to the CMS for a J-code for DEXTENZA on December 28, 2018 and expect to submit to the CMS for a standard J-code for our OTX-TP product candidate, if our clinical trials are successful and if our NDA filings and sNDA are approved by the FDA.

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. Among the provisions of ACA of importance to potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;

- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. However, the IPAB implementation has not been clearly defined. ACA provided that under certain circumstances, IPAB recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Other legislative changes have been proposed and adopted in the United States since ACA was enacted. For example, 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 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2024 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, 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 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 the President 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, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, among other things, amends the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". The Congress will likely consider other legislation to replace elements of the ACA during the next Congressional session.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs 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. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently

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. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than \$12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

Further, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state 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. For example, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state 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. At the federal level, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. For example, on May 11, 2018, the Administration issued a plan to lower drug prices. Under this blueprint for action, the Administration indicated that the Department of Health and Human Services (HHS) will: take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' ads to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases.

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.

## **Employees**

As of March 1, 2019, we had 167 full-time employees. Of these full-time employees, 123 employees are primarily engaged in research and development activities. 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.

## **Our Corporate Information**

We were incorporated under the laws of the State of Delaware in 2006. Our principal executive offices are located at 15 Crosby Drive, Bedford, MA 01730, and our telephone number is (781)357-4000. Our manufacturing and research and development operations are located at 36 Crosby Drive, Suite 101, Bedford, MA 01730. Our website address is [www.ocutx.com](http://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 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. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.*

### **Risks Related to Our Financial Position and Need for Additional Capital**

***We have 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 \$44.7 million for the year ended December 31, 2016, \$63.4 million for the year ended December 31, 2017, and \$60.0 million for the year ended December 31, 2018. As of December 31, 2018, we had an accumulated deficit of \$297.2 million. Through December 31, 2018, we have financed our operations primarily through private placements of our preferred stock, public offerings of our common stock 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, commercialization of ReSure Sealant and the potential commercial launch of DEXTENZA® for the treatment of ocular pain following ophthalmic surgery. Although we expect to generate revenue from sales of DEXTENZA following its commercial launch, 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:

- commercially launch DEXTENZA in the United States;
- continue to develop and expand our sales, marketing and distribution capabilities for DEXTENZA and any of our product candidates;
- continue to pursue the clinical development of our most advanced intracanalicular insert product candidates, OTX-TP and DEXTENZA in additional indications;
- continue clinical trials of our product candidates OTX-TIC and OTX-TKI;
- 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;
- 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 back-of-the-eye program and glaucoma intracameral implant program 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 the expected growth in personnel;
- renovate our new facility 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.

ReSure Sealant has been our only source of revenue from product sales. We do not expect sales of ReSure Sealant to generate revenue that is sufficient for us to achieve profitability. For us to become and remain profitable, we will need to succeed in developing and commercializing DEXTENZA or 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 completing the commercial launch of DEXTENZA, including by further developing our sales force, marketing and distribution capabilities;
- successfully completing clinical development of our product candidates;
- obtaining marketing approval for these product candidates, including DEXTENZA for additional indications;
- manufacturing at commercial scale, marketing, selling and distributing DEXTENZA or those 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, which we plan to commercially launch in the United States in 2019. However, the successful

commercialization of DEXTENZA in the United States is subject to many risks. We are currently undertaking our first commercial launch with DEXTENZA, and we may not be able to do so successfully or on the currently expected timeline or at all. 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 us. While we expect to commercially launch DEXTENZA for the treatment of ocular pain following ophthalmic surgery in 2019, we do not anticipate revenue from such sales of DEXTENZA will be sufficient for us to become profitable for several years, if ever.

We may never succeed in these activities and may never generate revenue that is sufficient or great enough 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 commercially launch DEXTENZA for the treatment of ocular pain following ophthalmic surgery, including expanding our product manufacturing, sales, marketing and distribution capabilities. We also expect to devote substantial financial resources as we conduct late stage clinical trials for our local programmed-release drug delivery product candidates, in particular OTX-TP and DEXTENZA for additional indications, 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 in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

As of December 31, 2018, we had cash and cash equivalents of \$54.1 million and outstanding debt of \$25.0 million. On December 21, 2018, we entered into a Third Amended and Restated Credit and Security Agreement, or the Credit Agreement, to refinance our existing secured term loan facility, which we refer to as our Credit Facility. The Credit Agreement increased the principal amount of the Credit Facility from \$18.0 million to \$25.0 million, all of which we drew at closing. A portion of the borrowings were used to pay off the approximately \$12.3 million outstanding principal balance under the prior agreement and to pay a loan origination fee. On March 1, 2019, we closed a private placement of \$37.5 million aggregate principal amount of our senior subordinated convertible notes, or the Convertible Notes, resulting in estimated net proceeds of approximately \$37.1 million. Based on our current plans and forecasted expenses, we believe that our existing cash and cash equivalents, as of December 31, 2018, along with the net proceeds from the sale of the senior subordinated notes, without giving effect to any potential payment under our Collaboration Agreement with Regeneron, will enable us to fund our operating expenses, debt service obligations and capital expenditure requirements into early 2020. 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 successfully 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 expected growth in personnel;
- the progress, costs and outcome of the clinical trials of our extended-delivery drug delivery product candidates, in particular OTX-TP and DEXTENZA for additional indications;
- the progress and status of our collaboration with Regeneron, including any development costs for which we reimburse Regeneron, the potential exercise by Regeneron of its option for a license for the development and potential commercialization of products containing our extended-delivery hydrogel formulation in combination with Regeneron's large molecule VEGF-targeting compounds, and our potential receipt of future milestone payments from Regeneron;
- the costs of advancing our internal development efforts for the back-of-the-eye small molecule TKI program through the remaining preclinical steps and potentially into an initial clinical trial;
- the scope, progress, costs and outcome of preclinical development and clinical trials of our other product candidates;
- the extent of our debt service obligations;
- the amounts we receive, if any, from Regeneron for option exercise, development, regulatory and sales milestones and royalty payments under our collaboration;
- 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, including the current lawsuits described under "Item 3—Legal 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 process that takes 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.

***We have included a paragraph relating to our ability to continue as a going concern in the footnotes of our audited consolidated financial statements included in this Annual Report on Form 10-K.***

Our audited consolidated financial statements for the period ended December 31, 2018 include a paragraph stating that our losses from operations and need for additional funding to finance our operations raise substantial doubt about our ability to continue as a going concern. If we are unable to obtain sufficient funding, our business, prospects, financial condition and results of operations will be materially and adversely affected and we may be unable to continue as a going concern. If we are unable to continue as a going concern, we may have to liquidate our assets and may receive less than the value at which those assets are carried on our consolidated financial statements, and it is likely that investors will lose all or a part of their investment. If we seek additional financing to fund our business activities in the future and there remains substantial doubt about our ability to continue as a going concern, investors or other financing sources may be unwilling to provide additional funding to us on commercially reasonable terms or at all.

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

Until such time, if ever, as we can generate product revenues sufficient to achieve profitability, we expect to finance our cash needs through equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements, royalty agreements, and marketing and distribution arrangements. We do not have any committed external source of funds other than the amounts we are entitled to receive from Regeneron for potential option exercise, development, regulatory and sales milestones and royalty payments under our collaboration. To the extent that we raise additional capital through the sale of 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 may limit our ability to obtain additional debt financing.

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

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

We have a significant amount of indebtedness. Under our Credit Facility, as amended on December 21, 2018, we had \$25.0 million, net of unamortized discount, of outstanding principal indebtedness. Under the amended Credit Facility, we are permitted to make interest-only payments until January 1, 2021, subject to potential extension to January 1, 2022 if net sales of DEXTENZA exceed \$40.0 million in the aggregate during any trailing twelve-month period. Our obligations under the Credit Facility are secured by all of our assets, including our intellectual property. The Credit Facility also includes a financial covenant requiring us to maintain at least \$5.0 million in cash and/or cash equivalents at all times as well as 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 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 Facility.

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 will reduce the amounts available to fund working capital, 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 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 potential payments under our collaboration with Regeneron 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 Facility 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 Facility 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 Facility and the pledge of our assets, including our intellectual property as collateral limit our ability to obtain additional debt financing.

***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, commercializing ReSure Sealant, and, beginning in 2019, commercializing DEXTENZA for the treatment of ocular pain following ophthalmic surgery. We have limited history of commercializing products, are still in the process of preparing for the commercial launch of DEXTENZA and, to date, have not generated revenue from the sale of DEXTENZA. 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 their use, we may invest our available cash 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, in particular DEXTENZA for additional indications and OTX-TP. 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 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 and product candidates for diseases and conditions of the front of the eye. In particular, we are investing substantial resources to complete the development of DEXTENZA for post-surgical ocular inflammation and allergic conjunctivitis and OTX-TP for glaucoma and ocular hypertension. 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 successful commercialization of DEXTENZA for the treatment of ocular pain following ophthalmic surgery and our obtaining marketing approval for and commercializing one or both of DEXTENZA for additional indications and OTX-TP.

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 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;
- 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 collaboration with Regeneron, 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 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, insert is 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, including our pilot studies for OTX-TP, 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 pain and inflammation 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 pain and inflammation 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 pain and inflammation in November 2016, which we plan to use 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 pain and inflammation, 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 timepoints, 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 December 2018 for the pain indication pursuant to the initial NDA, we submitted an NDA supplement, or sNDA, for DEXTENZA for the treatment of post-surgical ocular inflammation in January 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. Even if we obtain favorable clinical trial results in any additional Phase 3 clinical trials of DEXTENZA for allergic conjunctivitis, 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. Post-hoc analyses that we performed on the results of our 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.

We designed our Phase 2 clinical trials of OTX-TP for the treatment of glaucoma and ocular hypertension to assess clinically meaningful response to treatment, and did not power these trials to measure any efficacy endpoints with statistical significance. We reported topline efficacy results from our Phase 2b clinical trial of OTX-TP for the treatment of glaucoma and ocular hypertension in October 2015. OTX-TP did not achieve non-inferiority to timolol drops in our Phase 2b clinical trial. In this trial, on day 60 at the 8:00 a.m. time point, the OTX-TP group experienced a mean intraocular pressure, or IOP, lowering effect of 4.7 mmHg, compared with IOP lowering of 6.4 mmHg for the timolol arm. On day 90 at the 8:00 a.m. time point, the OTX-TP group experienced an IOP lowering effect of 5.1 mmHg, compared with an IOP lowering effect of 7.2 mmHg in the timolol arm. Also in this trial, on day 60, the OTX-TP group experienced a mean diurnal IOP lowering effect of 3.3 mmHg compared to baseline 5.9 mmHg compared for the timolol group. On day 90, the OTX-TP group experienced a mean diurnal IOP, or IOP, lowering effect of 3.6 mmHg compared to baseline, versus 6.3 mmHg for the timolol group. We expect that our planned Phase 3 clinical trials for OTX-TP, one of which we initiated during the third quarter of 2016, will be powered with an appropriate number of patients to measure with statistical significance whether OTX-TP is superior as compared to a placebo vehicle intracanalicular insert in the reduction of mean IOP from baseline at all of the nine diurnal time points at week 2, week 6 and week 12 visits. We completed an End-of-Phase 2 review with the FDA in April 2016 and initiated the first of two planned Phase 3 clinical trials of OTX-TP in September 2016. Based on discussions with the FDA, the Phase 3 clinical trial design has significant differences as compared to our completed Phase 2 clinical trials. In particular, the most notable changes from our first Phase 2 clinical trial to our first Phase 3 clinical trial are that our first Phase 3 clinical trial enrolls more subjects at a greater number of sites, has a different randomization, measures the primary efficacy endpoints on different days and at different timepoints, has a longer washout period. Despite these changes to our clinical trial protocol, we cannot be certain that our first Phase 3 clinical trial will be successful. We do not intend to initiate the second Phase 3 clinical trial until we receive data from the first Phase 3 clinical trial and discuss the results with the FDA. If we do not achieve our primary endpoint in the Phase 3 clinical trials with statistical significance or do not achieve a clinically meaningful reduction in IOP, we may not obtain marketing approval for OTX-TP.

In addition, post-hoc analyses that we performed on the results of our completed Phase 2b clinical trial may not be predictive of success in our planned Phase 3 clinical trials, including as a result of differences in trial design. 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.

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 the first Phase 3 trial of OTX-TP. If in our Phase 3 clinical trials the retention rates for our inserts 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 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. 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 typically conducted our initial and earlier stage clinical trials for our product candidates, including our intracanalicular insert product candidates, 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.

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 pain and inflammation 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 this indication. 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 a Phase 1 clinical trial of OTX-TKI outside the United States in 2018, and we dosed two patients in 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;
- 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.

Our first Phase 3 clinical trial of OTX-TP has reached the target enrollment of 550 patients at approximately 50 sites in the United States and will be the largest clinical trial we will have conducted to date. While now complete, enrollment in this trial was slower than projected. Our inability to enroll a sufficient number of patients in any of our other 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 local programmed-release drug delivery product candidates or 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 pain and inflammation 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 pain and inflammation, 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.

In our two pilot studies of OTX-TP for the treatment of glaucoma and ocular hypertension and our Phase 2a clinical trial of OTX-TP for the same indication, the most common adverse event was inflammatory reaction of the eyelids and ocular surface, which was noted in three patients in our pilot studies and in five patients in our Phase 2a clinical trial. No hyperemia-related adverse events were noted in any of the patients treated with OTX-TP in our Phase 2b clinical trial. There were no serious adverse events reported in our Phase 2b clinical trial; however, two

OTX-TP subjects and two timolol subjects discontinued study participation due to ocular adverse events. Ocular adverse events were reported for 39.4% and 37.5% of subjects in the OTX-TP and timolol groups, respectively. The most frequently reported ocular adverse events were dacryocanalculitis, or inflammation of the lacrimal ducts, acquired dacryostenosis, or closing of the tear ducts, and eyelid edema. In the Phase 2b clinical trial, inflammatory reaction at the administration site (punctal area) and lacrimal structure injury were each noted in one OTX-TP subject as compared to higher percentages in prior trials. In the Phase 2b trial, the majority of ocular adverse events, including the most frequently reported adverse events, were assessed by the investigators as treatment related. However, 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 all of our development efforts towards applying our proprietary, bioresorbable hydrogel technology platform to products and product candidates that are designed to provide extended delivery of 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 front-of-the-eye diseases and conditions. We are also developing 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 age related macular degeneration, or wet AMD. In October 2016, we entered into a 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 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. 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 our product candidate development programs and the potential commercialization of these products and product candidates, we will need to upgrade and expand our existing manufacturing facility, or relocate to another manufacturing facility, add manufacturing personnel and ensure that validated processes 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. 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 assurance standards applicable to medical device and drug manufacturers, such as cGMP, which is 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 assurance and the maintenance of records and documentation. Following an inspection by the FDA in March 2015, for example, we received an FDA Form 483 containing an inspectional observation relating to inadequate procedures for documenting follow-up information pertinent to the investigation of complaints and for evaluation of complaints for adverse event reporting. We submitted our response, which was accepted by the FDA, and updated our procedures. In addition, in February 2016, as part of the review of our NDA for DEXTENZA, the FDA conducted a pre-NDA approval inspection of our manufacturing operations. As a result of this inspection, we received an FDA Form 483 containing inspectional observations focused on process controls, analytical testing and physical security procedures related to manufacture of our drug product for stability and commercial production purposes. We addressed some observations before the inspection was closed and responded to the FDA with a corrective action plan to complete the inspection process. In July 2016, we received a Complete Response Letter, or CRL, from the FDA regarding our NDA for DEXTENZA. This CRL pertained to the deficiencies in manufacturing process and controls identified during the pre-NDA approval inspection of our manufacturing facility performed by the FDA New England District Office in February 2016 that were documented on the February Form 483. In January 2017, we resubmitted our NDA. Following a re-inspection of manufacturing operations by the FDA which was completed in May 2017, we received an FDA Form 483 containing inspectional observations focused on procedures for manufacturing processes and analytical testing related to the manufacture of drug product for commercial production. In July 2017, we received a second CRL from the FDA regarding our NDA for DEXTENZA for the treatment of post-surgical ocular pain, stating that the FDA had determined that it could not approve the NDA in its then-present form. FDA concerns included deficiencies in manufacturing processes and analytical testing related to manufacturing of drug product identified during the May 2017 pre-NDA approval inspection. In May 2017, we submitted our initial response to the Form 483 and, in November 2017, we submitted our responses to the FDA's remaining inspectional observations in an effort to close out the items identified in the Form 483. The remediation efforts we undertook in response to the FDA's inspectional observations and as a result of further internal review included upgrades to our manufacturing equipment and updates to our manufacturing processes and quality oversight. These changes were intended to resolve the FDA's outstanding concerns, including regarding the presence of particulate matter in certain manufactured lots of DEXTENZA, and enable us to consistently produce commercial lots and establish manufacturing processes sufficient for purposes of resubmission of our NDA. We resubmitted our NDA for DEXTENZA for the treatment of post-surgical ocular pain in June 2018, which was approved in December 2018. We may be subject to similar inspections and requirements in connection with subsequent applications for other product candidates or DEXTENZA for additional indications.

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 or error discovered after products have been produced and distributed also 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 \$15.3 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 supply of 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 expect to commercially launch DEXTENZA for the treatment of ocular pain in 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 either post-surgical ocular pain and inflammation following cataract surgery or allergic conjunctivitis, it is possible that the market acceptance of DEXTENZA could be less than if we had conducted such trials. Although market research we have commissioned indicates that a majority of ophthalmologists believe DEXTENZA could become a new standard of care 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 are in the early stages of building our own highly targeted, key account sales force for DEXTENZA that will focus on ambulatory surgical centers responsible for the largest volumes of cataract surgery. We commercially launched ReSure Sealant in February 2014 on a region by region basis in the United States through a network of independent distributors. In early 2017, we terminated these distributors and hired a contract sales force of four representatives to sell ReSure Sealant. We have subsequently terminated the agreement with the contract sales force to sell ReSure Sealant.

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. The building of such a sales force is not fully funded under the Company's current operating plan and is therefore subject to the risk of our ability to raise additional capital to support such an effort. We expect that a direct sales force will be required to effectively market and sell OTX-TP, if approved for marketing. We will also 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.

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 including our

collaboration with Regeneron, distribution or other marketing arrangements may also be lower than if we were to sell, market and distribute a product ourselves. On the other hand, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of any product or product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

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

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers 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, sustained 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 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. In addition, while DEXTENZA may be considered a post-surgical product in the same fashion as eye drops, it may instead be categorized as an inter-operative product. If DEXTENZA is categorized as an inter-operative product, it will not be subject to separate reimbursement, which could likewise limit its market acceptance.

We applied for a transitional pass-through reimbursement status, or C-code, on November 30, 2018 for DEXTENZA from the Centers for Medicare and Medicaid Services, or CMS, which we expect to receive in the middle of 2019. We expect pricing for DEXTENZA while in pass-through status to be approximately \$540 per surgery. We expect pass-through status would remain in effect for up to three years depending on when we apply for and receive this reimbursement code. We submitted an application to the CMS for a J-code for DEXTENZA on December 28, 2018, and expect to submit to the CMS for a standard J-code for our OTX-TP product candidate, if our clinical trials are successful and if our NDA filings and sNDA are approved by the FDA. There are no assurances that we will be successful in obtaining and retaining reimbursement for our products and product candidates.

***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, or Collaboration 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. Our ability to generate revenues from the Collaboration Agreement will depend on our and Regeneron's abilities to successfully perform the functions assigned to each of us under the Collaboration Agreement. We did not receive any upfront payment under the Collaboration Agreement, although 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. The option is exclusive until 12 months after Regeneron has received a product candidate in accordance with a collaboration plan and non-exclusive for an additional six months following the end of the exclusive period. In December 2017, we delivered to Regeneron the final formulation for Regeneron's initial preclinical tolerability study. Although we are engaged in ongoing discussions with Regeneron, Regeneron has not informed us of its decision to exercise the option. While we await a decision from Regeneron, we are not actively pursuing further formulation development or other preclinical testing under the Collaboration Agreement. Under the Collaboration Agreement, we are 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 million, which cap may be increased by up to \$5 million under certain circumstances. We are also entitled to receive under the terms of the Collaboration Agreement specified development, regulatory and sales milestone payments, as well as royalty payments.

If Regeneron has not exercised the option during the designated option period, the Collaboration Agreement will expire. If Regeneron exercises the option, the 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 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 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 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 our intravitreal implant product candidates 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 collaboration with Regeneron, 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 collaboration with Regeneron, 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 collaboration with Regeneron poses, and any future collaborations likely will pose a number of risks, including the following:

- collaborators have significant discretion in determining the amount and timing of efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of our products or product candidates that receive marketing approval or may elect not to continue or renew development or commercialization programs based on results of clinical trials or other studies, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could 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 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 are currently conducting 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 is 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 may 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 pain and inflammation following cataract surgery. However, we have relied and may continue to rely on third parties, such as contract research organizations, or CROs, to conduct future clinical trials of our product candidates, including OTX-TP for the treatment of glaucoma and ocular hypertension. 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. 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 expire between 2018 and 2019. 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 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 all patent rights and a significant portion of 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 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 are also aware of a U.S. patent with an expiration in 2020 with claims directed to formulations of hydrogels and which could be alleged to cover the hydrogel formulations used in our product candidates OTX-TP and OTX-MP. Based on the specifications and file history of that patent, we believe its claims should be construed with a scope that does not cover our product candidates. 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. Further, 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 have initiated both legal and administrative proceedings against these patents in order to show that DEXTENZA does not infringe the claims of these patents or that these patents are invalid.

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 all of our patent rights and a significant portion of 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 pain following ophthalmic surgery and have not received approval to market DEXTENZA for any other indication. 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 a CRL from the FDA. Following the July 2016 CRL, we resubmitted our NDA to the FDA in January 2017. After the May 2017 inspection, we received a Form 483 from the FDA focused on procedures from manufacturing processes and analytical testing related to the manufacture of drug product for commercial production. We received a CRL regarding these and other matters in July 2017. In November 2017, we submitted our complete responses to the FDA in an effort to close out the Form 483 deficiencies. We resubmitted our NDA for DEXTENZA for the treatment of post-surgical ocular pain in June

2018, and in December 2018 the FDA approved our NDA. We may be subject to similar inspections in the future for DEXTENZA or for other product candidates for which we seek FDA approval. 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.

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, 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 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, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of our products or product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our products or 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 our products or 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 PMA 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, the 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. 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 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. We do not have a fully developed compliance program and will need to establish a more robust compliance infrastructure to address our needs in this area. We may fail to establish appropriate compliance measures, and even with a stronger program in place, it is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in 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.

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 European Union 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 European Union, 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 our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities.

***Under the Cures Act and the Trump Administration's regulatory reform initiatives, the FDA's policies, regulations and guidance may be revised or revoked in a manner that could prevent, limit or delay regulatory approval of our product candidates, which would impact our ability to generate revenue.***

In December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and spur innovation, but its ultimate implementation is unclear. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. An under-staffed FDA could result in delays in the FDA's responsiveness or in its ability to review submissions or applications, issue regulations or guidance, or implement or enforce regulatory requirements in a timely fashion or at all. Moreover, on January 30, 2017, President Trump issued an Executive Order, applicable to all executive agencies, including the FDA, which requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This Executive Order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the Executive Order requires agencies to identify regulations to offset any incremental cost of a new regulation and approximate the total costs or savings associated with each new regulation or repealed regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within OMB on February 2, 2017, the administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. In addition, on February 24, 2017, President Trump issued an executive order directing each affected agency to designate an agency official as a "Regulatory Reform Officer" and establish a "Regulatory Reform Task Force" to implement the two-for-one provisions and other previously issued executive orders relating to the review of federal regulations, however it is difficult to predict how these requirements will be implemented, and the extent to which they

will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

***Current and future legislation 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.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and will stay in effect through 2024 unless additional Congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of 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 or product is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed 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.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

With enactment of the Tax Cuts and Jobs Act of 2017, or the 2017 Tax Act, which was signed by President Trump on December 22, 2017, Congress repealed the “individual mandate.” The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Moreover, on December 14, 2018, a United States District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseparable feature of the ACA, and therefore because the mandate was repealed as part of the 2017 Tax Act, the remaining provisions of the ACA are invalid as well. The Trump administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the same judge issued an order staying the judgment pending appeal. It is unclear how this decision and any subsequent appeals and other efforts to repeal and replace the ACA will impact the ACA and our business. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

Furthermore, since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs 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. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. The loss of the cost share reduction payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. Further, on June 14, 2018, the United States Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than \$12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

In addition, the CMS has recently 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 a definition of “price concession” in the regulations. It is unclear whether these proposed changes will 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. We continue to evaluate the effect that the ACA and its possible repeal and replacement has on our business.

We will continue to evaluate the effect that the ACA and its possible repeal and replacement could have on our business. It is possible that repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. While the timing and scope of any potential future legislation to repeal and replace ACA provisions is highly uncertain in many respects, it is also possible that some of the ACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with ACA coverage expansion provisions. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates.

The costs of prescription pharmaceuticals in the United States has also been the subject of considerable discussion in the United States, and members of Congress and the Administration have stated that they will address such costs through new legislative and administrative measures. The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. 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 candidates 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 ability to generate revenues and become profitable could be impaired.

In addition, on May 11, 2018, the Administration issued a plan to lower drug prices. Under this blueprint for action, the Administration indicated that the Department of Health and Human Services, or the HHS, will: take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' ads to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases.

At the same time, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly 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.

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.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. Increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

***Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.***

In some countries, such as the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we, or any current or future collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

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

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

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

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. 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.

***The comprehensive tax reform bill enacted in 2017 could adversely affect our business and 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, contains 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 net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such net operating losses may be carried forward indefinitely), the 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), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modification or repeal many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the 2017 Tax Act is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain how various states will respond to the 2017 Tax Act. The impact of the 2017 Tax Act on holders of our common stock is also uncertain and could be adverse. We urge our stockholders to consult with their legal and tax advisors with respect to the 2017 Tax Act and the potential tax consequences of investing in or holding our common stock

***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, 2018, we had federal and state net operating loss carryforwards of \$190.6 million, which begin to expire in 2026, and state net operating loss carryforwards of \$161.8 million, which begin to expire in 2026. As of December 31, 2018, we also had federal research and development tax credit carryforwards of \$7.0 million and state research and development tax credit carryforwards \$3.6 million, which begin to expire in 2026 and 2025, respectively. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset our future income tax liabilities. Under the 2017 Tax Act, federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited. It is uncertain how various states will respond to the 2017 Tax Act. If our ability to use our historical net operating loss and tax credit carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

**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 Amar Sawhney, Ph.D., our Chairman of the Board of Directors and former President and Chief Executive Officer, as well as the other 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 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.***

Although we had a reduction in workforce in 2017 primarily related to sales and marketing personnel, we expect our drug development, clinical, regulatory affairs, and manufacturing teams to grow in the short-term and may regrow our sales and marketing capabilities in the longer term as we commercialize DEXTENZA. 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. In 2016, we entered into a lease agreement for new general office research and development and manufacturing space. We relocated our corporate headquarters to the new leased premises during June 2017 and are evaluating the relocation of our manufacturing operations to the new leased premises. 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.

***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.

#### **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 are currently subject to legal actions and proceedings related to the decline in our stock price, which could distract our management and could result in substantial costs or large judgments against us.***

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 addition, 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 and August 2017, class action lawsuits were filed against us and certain of our current and former executive officers in the United States District Court for the District of New Jersey, which have subsequently been transferred to the United States District Court for the District of Massachusetts at our request. In addition, in July 2017, 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, in the United States District Court for the District of Massachusetts and in Massachusetts Superior Court (Suffolk County). These actions were re-filed in October and December 2017, were consolidated by court order in January 2018, and are now pending under one docket in Massachusetts Superior Court (Suffolk County). In January 2018, a third shareholder derivative action was filed against us, certain of our current and former executive officers, and certain of our current and former board members in the United States District Court for the District of Massachusetts. In February 2018, a fourth shareholder derivative action was filed against us, certain of our current and former executive officers, certain of our current and former board members, and two of our investors in the United States District Court for the District of Delaware. Due to the volatility in our stock price, we may be the target of similar litigation in the future.

In addition, we received a subpoena from the SEC in December 2017, requesting documents and information concerning DEXTENZA, including related communications with the FDA, investors and others. We received a second subpoena from the SEC in August 2018, requesting documents and information concerning our participation in two investor conferences in June 2017. We intend to fully cooperate with the SEC regarding this non-public, fact-finding inquiry.

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.

***An active trading market for our common stock may not be sustained.***

Our shares of common stock began trading on the Nasdaq Global Market on July 25, 2014. Given the limited trading history of our common stock, there is a risk that an active trading market for our shares will not be sustained, which could put downward pressure on the market price of our common stock and thereby affect the ability of our stockholders to sell their shares.

***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, 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, OTX-TP or our other product candidates. As described in “Item 3— Legal Proceedings,” we and certain of our current and former executive officers

and current and former board members have been named as defendants in purported class action lawsuits and derivative lawsuits. 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 an “emerging growth company” and a “smaller reporting company” and the reduced disclosure requirements applicable to such companies may make our common stock less attractive to investors.***

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company until December 31, 2019, provided that, if the market value of our common stock that is held by non-affiliates exceeds \$700 million as of any June 30 before that time or if we have annual gross revenues of \$1.07 billion or more in any fiscal year, we would cease to be an emerging growth company as of December 31 of the applicable year. We also would cease to be an emerging growth company if we issue more than \$1 billion of non-convertible debt over a three-year period. As an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We expect to continue to take advantage of some or all of the available exemptions.

We are also 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. Even after we no longer qualify as an emerging growth company, we may still qualify as a smaller reporting company, which would allow us to take advantage of many of the same exemptions from disclosure requirements. In addition to the above reduced disclosure requirements applicable to EGCs, 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;
- 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 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.

In addition, the JOBS Act also provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to delay such adoption of new or revised accounting standards, and, as a result, we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for public companies that are not emerging growth companies.

***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, and particularly after we are no longer an emerging growth company, we 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.

For as long as we remain an emerging growth company, we may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies as described in the preceding risk factor.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to 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 we will not 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 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 facility and any future debt agreements that we may enter into, may preclude us from paying dividends without the lenders' consent or at all. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.

**Item 1B. Unresolved Staff Comments**

None.

**Item 2. Properties**

Our facilities consist of office space, laboratory space and manufacturing facilities in Bedford, Massachusetts. We occupy approximately 91,000 square feet of space. The lease for approximately 71,000 square feet of space expires in July 2027 and the lease for approximately 20,000 square feet of space expires in 2023.

**Item 3. Legal Proceedings**

*Securities Class Actions*

On July 7, 2017, a putative class action lawsuit was filed against us and certain of our current and former executive officers in the United States District Court for the District of New Jersey, captioned *Thomas Gallagher v. Ocular Therapeutix, Inc., et al.*, Case No. 2:17-cv-05011. The complaint purports to be brought on behalf of shareholders who purchased our common stock between May 5, 2017 and July 6, 2017. The complaint generally alleges that we and certain of our current and former officers violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934, or the Exchange Act, and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning the Form 483 issued by the FDA related to DEXTENZA and our manufacturing operations for DEXTENZA. The complaint seeks unspecified damages, attorneys' fees, and other costs. On July 14, 2017, an amended complaint was filed; the amended complaint purports to be brought on behalf of shareholders who purchased our common stock between May 5, 2017 and July 11, 2017, and otherwise includes allegations similar to those made in the original complaint.

On July 12, 2017, a second putative class action lawsuit was filed against us and certain of our current and former executive officers in the United States District Court for the District of New Jersey, captioned *Dylan Caraker v. Ocular Therapeutix, Inc., et al.*, Case No. 2:17-cv-05095. The complaint purports to be brought on behalf of shareholders who purchased our common stock between May 5, 2017 and July 6, 2017. The complaint includes allegations similar to those made in the *Gallagher* complaint and seeks similar relief.

On August 3, 2017, a third putative class action lawsuit was filed against us and certain of our current and former executive officers in the United States District Court for the District of New Jersey, captioned *Shawna Kim v. Ocular Therapeutix, Inc., et al.*, Case No. 2:17-cv-05704. The complaint purports to be brought on behalf of shareholders who purchased our common stock between March 10, 2016 and July 11, 2017. The complaint includes allegations similar to those made in the *Gallagher* complaint and seeks similar relief.

On October 27, 2017, a magistrate judge for the United States District Court for the District of New Jersey granted the defendants' motion to transfer the above-referenced *Gallagher*, *Caraker*, and *Kim* litigations to the United States District Court for the District of Massachusetts. These matters were assigned the following docket numbers in the District of Massachusetts: 1:17-cv-12288 (*Gallagher*), 1:17-cv-12146 (*Caraker*), and 1:17-cv-12286 (*Kim*).

On March 9, 2018, the court consolidated the three actions and appointed co-lead plaintiffs and co-lead counsel for the consolidated action. On May 7, 2018, co-lead plaintiffs filed a consolidated amended class action complaint. The amended complaint makes allegations similar to those in the original complaints, against the same defendants, and seeks similar relief on behalf of shareholders who purchased our common stock between March 10, 2016 and July 11,

2017. The amended complaint generally alleges that defendants violated Sections 10(b) and/or 20(a) of the Exchange Act and Rule 10b-5 promulgated thereunder. On July 6, 2018, defendants filed a motion to dismiss the consolidated amended complaint. Plaintiffs' filed an opposition to the motion to dismiss on September 4, 2018, and defendants filed a reply on October 4, 2018. The court held oral argument on the motion to dismiss on February 6, 2019 and took the matter under advisement.

We deny any allegations of wrongdoing and intend to vigorously defend against these lawsuits.

#### *Shareholder Derivative Litigation*

On July 11, 2017, a purported shareholder derivative lawsuit was filed against certain of our current and former executive officers, certain current and former board members, and us as a nominal defendant, in the United States District Court for the District of Massachusetts, captioned *Robert Corwin v. Sawhney et al.*, Case No. 1:17-cv-11270. The complaint generally alleged that the individual defendants breached fiduciary duties owed to us by making allegedly false and/or misleading statements concerning the Form 483 related to DEXTENZA and our manufacturing operations for DEXTENZA. The complaint purported to assert claims against the individual defendants for breach of fiduciary duty, and sought to recover on behalf of us for any liability we incur as a result of the individual defendants' alleged misconduct. The complaint also sought contribution on behalf of us from all individual defendants for their alleged violations of Sections 10(b) and/or 20(a) of the Exchange Act and Rule 10b-5 promulgated thereunder. The complaint sought declaratory, equitable, and monetary relief, an unspecified amount of damages, with interest, and attorneys' fees and costs. On September 20, 2017, counsel for the plaintiff filed a notice of voluntary dismissal, stating that the plaintiff wished to coordinate his efforts and proceed in a consolidated fashion with the plaintiff in a similar derivative suit that was pending in the Superior Court of Suffolk County of the Commonwealth of Massachusetts captioned *Angel Madera v. Sawhney et al.*, Case No. 17-2273 (which is discussed in the paragraph immediately below) by filing an action in that court subsequent to the dismissal of this lawsuit. The *Corwin* lawsuit was dismissed without prejudice on September 21, 2017. On October 24, 2017, the plaintiff filed a new derivative complaint in Massachusetts Superior Court (Suffolk County), captioned *Robert Corwin v. Sawhney et al.*, Case No. 17-3425 (BLS2). The new *Corwin* complaint includes allegations similar to those made in the federal court complaint and asserts a derivative claim for breach of fiduciary duty against certain of our current and former officers and directors. The complaint also asserts an unjust enrichment claim against two additional defendants, SV Life Sciences Fund IV, LP and SV Life Sciences Fund IV Strategic Partners, LP. The complaint also names us as a nominal defendant.

On July 19, 2017, a second purported shareholder derivative lawsuit was filed against certain of our current and former executive officers, all current board members, one former board member, and us as a nominal defendant, in the Superior Court of Suffolk County of the Commonwealth of Massachusetts, captioned *Angel Madera v. Sawhney et al.*, Case No. 17-2273. The complaint included allegations similar to those made in the *Corwin* complaint. The complaint purported to assert derivative claims against the individual defendants for breach of fiduciary duty, unjust enrichment, abuse of control, gross mismanagement, and waste of corporate assets, and sought to recover on behalf of us for any liability we incur as a result of the individual defendants' alleged misconduct. The complaint sought declaratory, equitable, and monetary relief, an unspecified amount of damages, with interest, and attorneys' fees and costs. On November 6, 2017, the court dismissed this action without prejudice due to plaintiff's failure to complete service of process within the time permitted under applicable court rules. On December 21, 2017, the same plaintiff filed a new derivative complaint in the same court, captioned *Angel Madera v. Sawhney et al.*, Case No. 17-4126 (BLS2). The new *Madera* complaint is premised on substantially similar allegations as the previous complaint and purports to assert derivative claims against certain current and former executive officers and board members for breach of fiduciary duty, unjust enrichment, and waste of corporate assets, and names the Company as a nominal defendant. Like the new *Corwin* complaint, the new *Madera* complaint also asserts an unjust enrichment claim against two additional defendants, SV Life Sciences Fund IV, LP and SV Life Sciences Fund IV Strategic Partners, LP.

By order dated January 29, 2018, the court consolidated the state court *Corwin* and *Madera* complaints under the *Corwin* docket and appointed lead counsel for plaintiffs. On February 28, 2018, plaintiffs filed a consolidated amended complaint. The consolidated complaint names substantially the same defendants and is premised on substantially similar allegations as the previous *Corwin* and *Madera* complaints, asserting claims for breach of fiduciary duty against the individual defendants and unjust enrichment against the two SV entity defendants. On April 17, 2018, all defendants served a motion to dismiss the consolidated amended complaint. On June 22, 2018, plaintiffs served their opposition to the motion to dismiss and a cross-motion to stay the proceedings pending a decision on the motion to dismiss in the above-referenced securities class action in the District of Massachusetts. On July 30, 2018, the parties filed a joint

motion to stay the proceedings pending a decision on the motion to dismiss in the above-referenced securities class action in the District of Massachusetts. On August 3, 2018, the court granted the motion to stay.

On January 31, 2018, a third purported shareholder derivative suit was filed against certain of our current and former executive officers, certain current and former board members, and us as a nominal defendant, in the United States District Court for the District of Massachusetts, captioned *Brian Robinson v. Sawhney et al.*, Case. No. 1:18-cv-10199. The complaint includes allegations similar to those made in the *Corwin* and *Madera* complaints. The complaint does not name either SV Life Sciences Fund, IV, LP or SV Life Sciences Fund IV Strategic Partners, LP as defendants, and adds two former officers as defendants. The complaint purports to assert derivative claims against the individual defendants for breach of fiduciary duty, waste of corporate assets, and unjust enrichment, and seeks to recover on behalf of us for any liability we incur as a result of the individual defendants' alleged misconduct. The complaint seeks declaratory, equitable, and monetary relief, an unspecified amount of damages, with interest, and attorneys' fees and costs. On April 30, 2018, all defendants filed a motion to dismiss or stay the complaint. Plaintiff filed his opposition on June 22, 2018. On July 26, 2018, the parties filed a joint motion to extend the deadline for defendants to file their reply brief pending the potential substitution of the named shareholder plaintiff. On August 20, 2018, the parties filed a joint stipulation and proposed order regarding plaintiff's unopposed request to substitute a new shareholder plaintiff and the parties' joint request that the court stay the proceedings pending a decision on the motion to dismiss in the above-referenced securities class action in the District of Massachusetts. On September 4, 2018, the court entered the requested order substituting the named plaintiff and staying the matter.

On February 16, 2018, a fourth purported shareholder derivative suit was filed against certain of our current and former executive officers, certain current and former board members, and us as a nominal defendant, in the United States District Court for the District of Delaware, captioned *Terry Kelly v. Sawhney et al.*, Case. No. 1:18-cv-00277. The complaint includes allegations similar to those made in the *Corwin* and *Madera* complaints. The complaint purports to assert derivative claims against the individual defendants for breach of fiduciary duty, unjust enrichment, and waste of corporate assets, and seeks to recover on behalf of us for any liability we incur as a result of the individual defendants' alleged misconduct. The complaint also asserts an unjust enrichment claim against SV Life Sciences Fund IV, LP and SV Life Sciences Fund IV Strategic Partners, LP. The complaint seeks declaratory, equitable, and monetary relief, an unspecified amount of damages, with interest, and attorneys' fees and costs. On June 11, 2018, the parties filed a stipulation staying the lawsuit pending final judgment in the consolidated derivative action pending in Massachusetts state court under the *Corwin* docket, described above. The court entered an order staying the case on June 12, 2018.

We deny any allegations of wrongdoing and intend to vigorously defend against these lawsuits.

In addition, we have received a subpoena from the SEC, dated December 15, 2017, requesting documents and information concerning DEXTENZA (dexamethasone insert) 0.4mg, including related communications with the U.S. Food and Drug Administration, investors and others. The Company received a second subpoena from the SEC on August 21, 2018, requesting documents and information concerning its participation in two investor conferences in June 2017. We intend to fully cooperate with the SEC regarding this non-public, fact-finding inquiry. The SEC has informed us that this inquiry should not be construed as an indication that any violations of law have occurred or that the SEC has any negative opinion of any person, entity or security.

We are unable to predict the outcome of these lawsuits or proceedings at this time. Moreover, any conclusion of these matters in a manner adverse to us and for which we incur substantial costs or damages not covered by our directors' and officers' liability insurance would have a material adverse effect on our financial condition and business. In addition, the proceedings could adversely impact our reputation and divert management's attention and resources from other priorities, including the execution of business plans and strategies that are important to our ability to grow our business, any of which could have a material adverse effect on our business.

**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, 2019, there were approximately 34 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, 2018 that were not registered under the Securities Act of 1933, as amended, or the Securities Act, and that have not otherwise been described in an Annual Report on Form 10-K or a Quarterly Report on Form 10-Q.

#### **Purchase of Equity Securities**

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

**Item 6. Selected Financial Data**

The following selected financial data should be read together with our consolidated financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K and the “Management’s Discussion and Analysis of Financial Condition and Results of Operations” section of this Annual Report on Form 10-K. We have derived the statements of operations data for the years ended December 31, 2018, 2017, and 2016, and the balance sheet data as of December 31, 2018 and 2017 from our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K. We have derived the statements of operations data for the years ended December 31, 2015 and 2014 and the balance sheet data as of December 31, 2016, 2015 and 2014 from our audited consolidated financial statements not included in this Annual Report on Form 10-K. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period.

	Year Ended December 31,				
	2018	2017	2016	2015	2014
(in thousands, except per share data)					
<b>Statement of Operations Data:</b>					
Revenue:					
Product revenue	\$ 1,990	\$ 1,923	\$ 1,845	\$ 1,354	\$ 460
Collaboration revenue	—	—	42	396	312
Total revenue	<u>1,990</u>	<u>1,923</u>	<u>1,887</u>	<u>1,750</u>	<u>772</u>
Costs and operating expenses:					
Cost of product revenue	465	457	443	319	91
Research and development	36,915	30,880	27,065	26,611	18,880
Selling and marketing	4,942	17,000	6,701	3,852	1,982
General and administrative	18,786	15,509	11,004	9,165	6,913
Total costs and operating expenses	<u>61,108</u>	<u>63,846</u>	<u>45,213</u>	<u>39,947</u>	<u>27,866</u>
Loss from operations	<u>(59,118)</u>	<u>(61,923)</u>	<u>(43,326)</u>	<u>(38,197)</u>	<u>(27,094)</u>
Other income (expense):					
Interest income	879	424	304	166	7
Interest expense	(1,739)	(1,892)	(1,680)	(1,724)	(1,119)
Other income (expense), net	—	5	(1)	7	(442)
Total other expense, net	<u>(860)</u>	<u>(1,463)</u>	<u>(1,377)</u>	<u>(1,551)</u>	<u>(1,554)</u>
Net loss	<u>(59,978)</u>	<u>(63,386)</u>	<u>(44,703)</u>	<u>(39,748)</u>	<u>(28,648)</u>
Accretion of redeemable convertible preferred stock to redemption value	—	—	—	—	(11)
Net loss attributable to common stockholders	<u>\$(59,978)</u>	<u>\$(63,386)</u>	<u>\$(44,703)</u>	<u>\$(39,748)</u>	<u>\$(28,659)</u>
Net loss per share attributable to common stockholders, basic and diluted	<u>\$ (1.57)</u>	<u>\$ (2.20)</u>	<u>\$ (1.80)</u>	<u>\$ (1.71)</u>	<u>\$ (2.69)</u>
Weighted average common shares outstanding, basic and diluted	<u>38,115</u>	<u>28,818</u>	<u>24,816</u>	<u>23,244</u>	<u>10,653</u>
As of December 31,					
(in thousands)					
<b>Balance Sheet Data:</b>					
Cash, cash equivalents and marketable securities	\$ 54,062	\$ 41,538	\$ 68,145	\$ 105,064	\$ 74,828
Working capital	47,034	29,914	61,598	101,605	70,309
Total assets	73,043	55,431	74,939	110,306	78,193
Long-term debt, net of discount, including current portion	24,788	18,016	15,643	15,272	14,865
Total stockholders’ equity	35,875	26,147	52,008	89,588	58,696

## 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 of varying duration in our product candidates.

We currently incorporate U.S. Food and Drug Administration, or FDA, approved therapeutic agents, 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 intracanalicular inserts, intracameral implants and intravitreal implants. We have products and product candidates in clinical and preclinical development applying this technology to treat post-surgical ocular pain and inflammation, allergic conjunctivitis, dry eye disease, glaucoma and ocular hypertension, and wet age-related macular degeneration, or wet AMD, among other conditions.

In November 2018 the FDA approved our new drug application, or NDA, for DEXTENZA<sup>®</sup> (dexamethasone ophthalmic insert) 0.4mg for intracanalicular use for the treatment of ocular pain following ophthalmic surgery. DEXTENZA is the first FDA-approved intracanalicular insert delivering dexamethasone to treat post-surgical ocular pain for up to 30 days with a single administration. We are also evaluating DEXTENZA for the treatment of post-surgical ocular inflammation and allergic conjunctivitis.

We are developing our product candidate OTX-TP (intracanalicular travoprost insert) for the reduction of intraocular pressure, or IOP, in patients with glaucoma and ocular hypertension. Both DEXTENZA and OTX-TP are local programmed-release, drug-eluting, preservative-free intracanalicular inserts that are placed into the canaliculus through a natural opening called the punctum located in the portion of the lower eyelid near the nose.

Our earlier stage assets include two development programs that have initiated clinical trials: OTX-TIC, an intracameral travoprost implant for the reduction of IOP in patients with glaucoma and ocular hypertension when greater IOP reduction is needed, and OTX-TKI, an intravitreal injection by fine gauge needle of a hydrogel, anti-angiogenic formulation of a tyrosine kinase inhibitor, or TKI, for the treatment of wet AMD. 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 VEGF inhibitor, aflibercept, currently marketed under the brand name Eylea.

In addition to our ongoing drug product development, we currently market ReSure<sup>®</sup> Sealant, a hydrogel ophthalmic wound sealant approved by the FDA to seal corneal incisions following cataract surgery. ReSure Sealant is the first and only surgical sealant to be approved by the FDA for ophthalmic use.

### ***DEXTENZA<sup>®</sup> (dexamethasone ophthalmic insert)***

DEXTENZA incorporates the FDA-approved corticosteroid dexamethasone as an active pharmaceutical ingredient into a hydrogel, drug-eluting intracanalicular insert. In November 2018 the FDA approved our NDA for DEXTENZA for the treatment of post-surgical ocular pain. In connection with our commercial launch of DEXTENZA, we intend to build our own highly targeted, key account sales force that will focus on the ambulatory surgical centers responsible for

the largest volumes of cataract surgery. Following our receipt of FDA approval, we submitted on November 30, 2018 an application for a C-code for transitional pass-through payment status and also submitted on December 28, 2018 an application for a J-code for permanent payment status.

A C-code is a unique temporary pricing code established by the Center for Medicare & Medicaid Services (CMS), for the Prospective Payment System and is only valid for claims for hospital outpatient department services and procedures. A J-Code is a permanent code used to report drugs that ordinarily cannot be self-administered.

We have completed three Phase 3 clinical trials of DEXTENZA for the treatment of post-surgical ocular pain and inflammation. The data from two of these three completed Phase 3 clinical trials and a prior Phase 2 clinical trial were used to support our NDA for post-surgical ocular pain. We submitted an NDA supplement, or sNDA, for DEXTENZA for the treatment of post-surgical ocular inflammation in January 2019 and expect to hear back from the Food and Drug Administration, or FDA, within approximately ten months. We have also completed two Phase 3 clinical trials of DEXTENZA for the treatment of allergic conjunctivitis and a Phase 2 clinical trial of DEXTENZA for the treatment of dry eye disease.

#### ***OTX-TP (intracanalicular travoprost insert)***

Our product candidate OTX-TP incorporates travoprost, an FDA-approved prostaglandin analog as its active pharmaceutical ingredient that reduces elevated IOP, into a hydrogel, drug-eluting intracanalicular insert. This preservative-free insert is designed to elute drug for up to 90 days. OTX-TP is being developed as a treatment to lower IOP in patients with primary open angle glaucoma and ocular hypertension. We reported topline results from a Phase 2b clinical trial for this indication in October 2015. We completed an End-of-Phase 2 review with the FDA in April 2016 and initiated the first of two planned Phase 3 clinical trials of OTX-TP in September 2016. Our first Phase 3 trial has completed the target enrollment of 550 patients at approximately 50 sites in the United States. We have completed our target enrollment and are not screening any additional subjects. Based on discussions with the FDA, the first Phase 3 clinical trial design includes an OTX-TP treatment arm and a placebo-controlled comparator arm that uses a non-drug eluting hydrogel intracanalicular insert. The primary efficacy endpoint is superiority in the reduction of IOP from baseline in the OTX-TP treatment arm compared to the placebo arm at three diurnal time points at each of three measurement dates, 2, 6 and 12 weeks. We expect that the FDA will require that OTX-TP show both a statistically superior reduction of IOP compared to the placebo and a clinically meaningful reduction of IOP prior to granting marketing approval. We expect topline efficacy data from the first Phase 3 clinical trial in the first half of 2019. We do not intend to initiate the second Phase 3 clinical trial until we review and discuss with the FDA the data from the first Phase 3 clinical trial. Given the anticipated use of OTX-TP as a chronic therapy, we intend to generate six-month (300 patients) and one-year (100 patients) safety data to support our product registration. In order to meet these targets, we began enrollment in the open-label one-year safety extension study in July 2018.

#### ***OTX-TIC (intracanalicular travoprost implant)***

OTX-TIC is our product candidate for glaucoma patients in need of a more significant reduction in IOP and ocular hypertension. 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. Preclinical studies to date have demonstrated reduction of IOP and pharmacokinetics in the aqueous humor that suggest a pharmacodynamic response of IOP reduction in humans. Our investigational new drug application, or IND, for our U.S. trial became effective in the first quarter of 2018, and we dosed the first patient in May 2018. This clinical trial is a multi-center, open-label, dose-escalation, proof-of-concept study designed to evaluate the safety, durability, tolerability, and efficacy of OTX-TIC in patients with primary open-angle glaucoma or ocular hypertension. We anticipate presenting initial results from this clinical trial at the Association of Research and Vision of Ophthalmology meeting in April 2019.

#### ***Back-of-the-Eye Programs***

We are engaged in the development of formulations 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 initial development efforts are focused on the use of our extended-delivery hydrogel in combination with anti-angiogenic drugs, such as protein-

based anti-VEGF drugs, or small molecule drugs, such as TKIs, for the treatment of retinal diseases such as wet AMD, retinal vein occlusion and diabetic macular edema. Our initial goal for these programs is to provide extended delivery over a four to nine month period thereby reducing the frequency of the current monthly or bi-monthly immediate release intravitreal injection regimen for wet AMD and other retinal diseases.

#### *OTX-TKI (intravitreal tyrosine kinase inhibitor implant)*

OTX-TKI is a preformed, bioresorbable hydrogel fiber incorporating a small molecule TKI with anti-angiogenic properties delivered by intravitreal injection. TKIs have shown promise in the treatment of wet AMD. In May 2017, we reported data from preclinical studies evaluating the efficacy, tolerability and pharmacokinetics of OTX-TKI. In this study, OTX-TKI was well-tolerated, and high levels of drug were maintained in the tissue for up to twelve months in Dutch belted rabbits. In the first quarter of 2019, we dosed two patients in a Phase 1 clinical trial in Australia. This clinical trial is a multi-center, open-label study designed to evaluate the safety, durability and tolerability of OTX-TKI. We also plan to evaluate biological activity by following visual acuity over time and measuring retinal thickness using standard optical coherence tomography.

#### *Regeneron Collaboration*

In October 2016, we entered into a strategic collaboration, option and license agreement, or Collaboration Agreement, with Regeneron for the development and potential commercialization of products using our hydrogel 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. 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 have 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. A joint research committee comprised of an equal number of representatives from each of Regeneron and us is responsible for reviewing, approving and overseeing the parties' research and development activities with respect to licensed product candidates and making any modifications to those activities. In general, Regeneron has final decision-making authority over matters on which the joint research committee deadlocks, following escalation to designated executive officer representatives of the parties, except for matters that would impose a material increase in costs or obligations on us beyond those costs and obligations included in the mutually agreed collaboration plan. 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 Licensed Products. We refer to the formulation we are developing with Regeneron as OTX-IVT.

Under the terms of the Collaboration Agreement, Regeneron is responsible for funding an initial preclinical tolerability study, which it initiated in early 2018. If the Option is exercised, Regeneron will 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 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. We are also eligible to receive up to \$145 million per Licensed Product upon the achievement of specified development and regulatory milestones, including successful results from the first-in-human clinical trial, \$100 million per Licensed Product upon first commercial sale of such Licensed Product and up to \$50 million based on the achievement of specified sales milestones for all 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 Licensed Products.

### *ReSure® Sealant*

Following our receipt of FDA approval for ReSure Sealant, we commercially launched this product in the United States in 2014. ReSure Sealant is approved to seal corneal incisions following cataract surgery and is the first and only surgical sealant to be approved by the FDA for ophthalmic use. 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. While ReSure Sealant remains commercially available in the United States, there is no sales support currently provided to the product. We have received only limited revenues from ReSure Sealant to date and anticipate only limited sales for 2019.

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 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 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. 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. We have provided regular periodic reports to the FDA on the progress of this post-approval study.

We received a warning letter from the FDA in October 2018 relating to our compliance with data collection and information reporting obligations in the Device Exposure Registry Study. The FDA warning letter refers to a lack of progress with the enrollment and related data collection and information reporting obligations for a required post-approval trial. In November 2018, we appealed this warning letter. On December 26, 2018, the FDA rejected our appeal. 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. We continue to work with FDA to find a path to evaluate the incidence of endophthalmitis in patients receiving ReSure Sealant. ReSure Sealant currently remains commercially available in the United States, though there is no sales support provided to the product at this time. We have received only limited revenues from ReSure Sealant to date and anticipate only limited sales for 2019.

### ***Additional Potential Areas for Growth***

In addition to our focus on formulating, developing and commercializing innovative therapies for diseases and conditions of the eye, we are also assessing the potential use of our hydrogel platform technology in other areas of the body.

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 amends and restates in full the Company's prior amended and restated license agreement with Incept, dated as of January 27, 2012, to expand the scope of the Company's 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.

### **Financial Position**

We have generated limited revenue to date. In the first quarter of 2014, we began recognizing revenue from sales of ReSure Sealant. All of our local programmed-release drug delivery products are in various phases of clinical and preclinical development. We do not expect sales of ReSure Sealant to generate revenue that is sufficient for us to achieve profitability. Instead, our ability to generate product revenue sufficient to achieve profitability will depend heavily on our obtaining marketing approval for and commercializing products with greater market potential, including one or both of DEXTENZA and OTX-TP. Since inception, we have incurred significant operating losses. Our net losses were \$60.0 million, \$63.4 million and \$44.7 million for the years ended December 31, 2018, 2017 and 2016, respectively. As of December 31, 2018, we had an accumulated deficit of \$297.2 million.

Our total cost and operating expenses were \$61.1 million, \$63.8 million and \$45.2 million for the years ended December 31, 2018, 2017 and 2016, respectively, including \$7.5 million, \$7.3 million and \$6.0 million, respectively, in non-cash stock-based compensation expense. Our operating expenses have grown as we continue to pursue the clinical development of OTX-TP and DEXTENZA for additional indications; continue the research and development of our other product candidates; continue the internal development of our intravitreal hydrogel formulation for the local programmed-release of protein-based or small molecule anti-angiogenic drugs, such as OTX-IVT and OTX-TKI for the treatment of wet AMD and other back-of-the-eye diseases; and seek marketing approval for any such product candidate for which we obtain favorable pivotal clinical trial results. In August 2017, we updated our DEXTENZA commercial plans and expect to realize savings in operating expenses, including reduced personnel costs, as a result of streamlining headcount, as part of an initiative to enhance operations and reduce expenses. As a result, we expect to incur substantial sales and marketing expenses in connection with the 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.

Although, we expect to generate revenue from sales of DEXTENZA and potentially ReSure Sealant, we will need to obtain substantial additional funding in connection with our continuing operations and supporting the commercial launch of DEXTENZA. If we are unable to access our borrowing capacity or 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 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, 2015, we raised \$132.0 million through the sale of common stock in various offerings. 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. Through February 25, 2019, we have 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, commission and other offering expenses. On February 28, 2019, pursuant to the 2016 Sales Agreement, we delivered a termination notice to Cantor, terminating the 2016 Sales Agreement. In January 2017, we completed a follow-on offering of our common stock at a public offering price of \$7.00 per share. The offering consisted of 3,571,429 shares of common stock sold by us. We received net proceeds from the follow-on offering of approximately \$23.3 million after deducting underwriting discounts, commissions and expenses. In January 2018, we completed a follow-on offering of our common stock at a public offering price of \$5.00 per share. The offering consisted of 7,475,000 shares of common stock sold by us, including those shares sold in connection with the exercise by the underwriter of its option to purchase additional shares. We received net proceeds from the follow-on offering of approximately \$35.1 million after deducting underwriting discounts and commissions. In March 2019, we completed a private placement of senior subordinated convertible notes and received net proceeds from the offering of \$37.1 million. Based on our current plans and forecasted expenses, we believe that our existing cash and cash equivalents, as of December 31, 2018, together with the net proceeds of our private placement of Convertible Notes, without giving effect to any potential payment under our Collaboration Agreement with Regeneron, will enable us to fund our operating expenses, debt service obligations and capital expenditure requirements into early 2020. 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. See “—Liquidity and Capital Resources.”

## Financial Operations Overview

### Revenue

From our inception through December 31, 2018, we have generated limited amounts of revenue from the sales of our products. Our ReSure Sealant product received premarket approval, or PMA, from the FDA in January 2014. We commenced sales of ReSure Sealant in the first quarter of 2014, have received only limited revenues from ReSure Sealant to date and anticipate only limited sales for 2019. ReSure Sealant is currently our only source of revenue from product sales. We may generate revenue in the future if we successfully develop 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.

### Operating Expenses

#### 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 table below summarizes our research and development expenses incurred by product development program:

	Year Ended December 31,		
	2018	2017	2016
	(in thousands)		
ReSure Sealant	\$ 189	\$ 126	\$ 236
DEXTENZA for post-surgical ocular pain and inflammation	1,085	1,319	2,686
DEXTENZA for allergic conjunctivitis	20	621	2,815
DEXTENZA for dry eye disease	—	6	101
OTX-TP for glaucoma and ocular hypertension	5,305	5,288	1,941
Unallocated expenses	30,316	23,520	19,286
Total research and development expenses	<u>\$36,915</u>	<u>\$30,880</u>	<u>\$27,065</u>

We expect that our expenses will increase in connection with our ongoing activities. We estimate that in 2019, we will incur approximately \$58.0 million to \$64.0 million of research and development expenses, including costs related to clinical trials and other research and development activities. Of this amount, we estimate we will incur approximately \$13.0 million to \$17.0 million of external research and development expenses related to clinical trial and regulatory costs for DEXTENZA, OTX-TP, OTX-TKI and product candidates and approximately \$45.0 million to \$47.0 million of other research and development activities that we do not expect to track by program. In addition, we expect to purchase \$5.0 million to \$6.0 million in manufacturing and research and development capital equipment for our new facility.

We estimate that we will incur external research and development expenses for 2019, as follows:

- approximately \$4.0 million to \$5.0 million for DEXTENZA for post-surgical ocular pain and inflammation;
- approximately \$4.0 million to \$5.0 million for OTX-TP and OTX-TIC for glaucoma and ocular hypertension;
- approximately \$2.0 million to \$3.0 million for OTX-TKI for Wet AMD; and
- approximately \$3.0 million to \$4.0 million for other external research and development activities.

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 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;
- significant and changing government regulation; and
- the timing, receipt and terms of any marketing approvals.

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.

### *General and Administrative Expenses*

General and administrative expenses consist primarily of salaries and related costs, including stock-based compensation, for personnel in executive, finance and administrative functions. General and administrative expenses also include 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 increase our headcount to support our continued development and commercialization of our product candidates. We also anticipate to 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, 2018, 2017 and 2016, we incurred selling and marketing expense in connection with ReSure Sealant, which we began commercializing in the first quarter of 2014. In 2019, we plan to launch DEXTENZA. As a result, our selling and marketing expenses will increase.

### **Other Income (Expense)**

Interest income consists primarily of interest income earned on cash and cash equivalents. In each of 2018, 2017, and 2016, our interest income has not been significant due to the low rates of interest being earned on our invested balances.

Interest expense consists of interest expense on our debt. We borrowed \$15.0 million in aggregate principal amount in April 2014. In December 2015, we amended our credit facility to increase the aggregate principal amount 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 facility to increase the aggregate principal amount 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 our credit facility to increase the aggregate principal amount to \$25.0 million, extend the interest-only payment period through December 2020, and extend the maturity date to December 2023.

Other Income (Expense), Net. In 2014, other income (expense), net consisted primarily of the gain or loss associated with the change in the fair value of our preferred stock warrant liability and small amounts of miscellaneous income and expense items unrelated to core operations. We issued warrants for the purchase of our redeemable convertible preferred stock that we believed were financial instruments that could require a transfer of assets because of the redemption feature of the underlying stock. Therefore, we classified these warrants as liabilities and they were remeasured to fair value at each reporting period, and we recorded the changes in the fair value as a component of other income (expense), net. Upon the closing of our IPO in July 2014, the underlying redeemable convertible preferred stock was converted into common stock, the preferred stock warrants became exercisable for common stock instead of preferred stock, and the fair value of the warrant liability became fixed as of that date and was reclassified to additional paid-in capital. In 2016, 2017 and 2018, other income (expense), net consists of small amounts of miscellaneous income and expense items unrelated to our core operations.

### **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***

On January 1, 2018, we adopted the new revenue standard, Accounting Standards Codification (“ASC”) 606 – *Revenue from Contracts with Customers*, which amended revenue recognition principles and provides a single, comprehensive set of criteria for revenue recognition within and across all industries. The adoption of the new revenue standard did not have a material impact on our consolidated financial statements. This new revenue standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. The new revenue standard provides a five-step framework whereby revenue is recognized when control of promised goods or services is transferred to a customer at an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of the new revenue standard, we perform 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) we satisfy a performance obligation. We only apply the five-step model to contracts when collectability of the consideration to which we are entitled in exchange for the goods or services we transfer to the customer is determined to be probable. At contract inception, once the contract is determined to be within the scope of the new revenue standard, we assess whether the goods or services promised within each contract are distinct and, therefore, represent a separate performance obligation. Goods and services that are determined not to be distinct are combined with other promised goods and services until a distinct bundle is identified. We then allocate the transaction price (the amount of consideration we expect to be entitled to from a customer in exchange for the promised goods or services) to each performance obligation and recognize the associated revenue when (or as) each performance obligation is satisfied.

Amounts are recorded as accounts receivable when our right to consideration is unconditional. We do not assess whether a contract has a significant financing component if the expectation at contract inception is that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less. We expense incremental costs of obtaining a contract as and when incurred if the expected amortization period of the asset that we would have recognized is one year or less or the amount is immaterial.

We recognize revenue on product sales at the time control of the product transfers to the customer. In substantially all of our arrangements, title of its products transfers at shipping point and, as a result, we determined control transfers at the point of shipment. In more limited cases, there are destination-based shipping terms and, thus, control is deemed to transfer when the product arrives at the customer site. Incremental costs of obtaining a contract are expensed as and when incurred if the expected amortization period of the asset that would have been recognized is one year or less. Shipping and handling costs are included as a component of cost of product revenue.

Payment terms and conditions vary among our customers, although terms generally include a requirement of payment within 30 days of product shipment. Prior to providing payment terms to customers, an evaluation of the customer’s credit risk is performed. Returns and customer credits are infrequent and insignificant and are recorded as a reduction to sales. Rights of return are not included in sales arrangements and, therefore, there is minimal variable consideration included in the transaction price of our products.

### ***Accrued Research and Development Expenses***

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated costs incurred for the services when we have not yet been invoiced or otherwise notified of the actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advanced payments. We make estimates of our accrued expenses as of each balance sheet date in our consolidated financial statements based on facts

and circumstances known to us at that time. Examples of estimated accrued research and development expenses include fees paid to:

- investigative sites or other providers in connection with clinical trials;
- vendors in connection with preclinical development activities;
- CROs in connection with clinical trials; and
- vendors related to product manufacturing, development and distribution of clinical supplies.

We base our expenses related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple CROs that conduct and manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed, enrollment of patients, number of sites activated and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period. To date, we have not made any material adjustments to our prior estimates of accrued research and development expenses.

### ***Stock-Based Compensation***

We measure 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. We recognize the fair value of the awards as expense, net of estimated forfeitures, over the requisite service period, which is generally the vesting period of the respective award. We apply the straight-line method of expense recognition to all awards with service-only conditions.

For stock-based awards granted to consultants and nonemployees, we recognize compensation expense over the period during which services are rendered by such consultants and nonemployees until completed. At the end of each financial reporting period prior to completion of the service, we remeasure the fair value of these awards using the then-current fair value of our common stock and updated assumption inputs in the Black-Scholes option-pricing model.

We estimate the fair value of each stock option grant using the Black-Scholes option-pricing model. Use of this model requires that we make assumptions as to the volatility of our common stock, the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options and our expected dividend yield. Prior to our IPO, we had been a private company and lacked company-specific historical and implied volatility information. Therefore, we estimate our expected volatility based on the historical volatility of a publicly traded group of peer companies and expect to continue to do so until such time as we have adequate historical data regarding the volatility of our publicly traded stock price. Beginning in 2016, we estimate our expected volatility using a weighted average of the historical volatility of our publicly traded peer companies and the volatility of our common stock, and expect to continue to do so until such time as we have adequate historical data regarding the volatility of our traded stock price. We use the simplified method prescribed by Securities and Exchange Commission Staff Accounting Bulletin No. 107, Share-Based Payment, to calculate the expected term of options granted to employees and directors. We base the expected term of options granted to consultants and nonemployees on the contractual term of the options. We determine the risk-free interest rate 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 we have never paid cash dividends and do not expect to pay any cash dividends in the foreseeable future.

The assumptions we used to determine the fair value of stock options granted to employees and directors are as follows, presented on a weighted average basis:

	<u>Year Ended December 31,</u>		
	<u>2018</u>	<u>2017</u>	<u>2016</u>
Risk-free interest rate	2.65 %	2.00 %	1.42 %
Expected term (in years)	6	6	6
Expected volatility	102 %	102 %	85 %
Expected dividend yield	— %	— %	— %

These assumptions represented our best estimates, but the estimates involve inherent uncertainties and the application of our judgment. As a result, if factors change and we use significantly different assumptions or estimates, our stock-based compensation expense could be materially different. We recognize compensation expense for only the portion of awards that are expected to vest. In developing a forfeiture rate estimate for pre-vesting forfeitures, we have considered our historical experience of actual forfeitures. If our future actual forfeiture rate is materially different from our estimate, our stock-based compensation expense could be significantly different from what we have recorded in the current period.

### ***JOBS Act; Smaller Reporting Company Status***

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company for up to five years. As an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We expect to continue to take advantage of some or all of the available exemptions.

We are also 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. Even after we no longer qualify as an emerging growth company, we may still qualify as a smaller reporting company, which would allow us to take advantage of many of the same exemptions from disclosure requirements. In addition to the above reduced disclosure requirements applicable to EGCs, 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;
- 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.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to delay such adoption of new or revised accounting standards, and, as a result, we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for public companies that are not emerging growth companies.

## Results of Operations

### Comparison of the Years Ended December 31, 2018 and December 31, 2017

The following table summarizes our results of operations for the years ended December 31, 2018 and 2017:

	Year Ended		Increase (Decrease)
	December 31, 2018	2017	
	(in thousands)		
Revenue:			
Product revenue	\$ 1,990	\$ 1,923	\$ 67
Total revenue	1,990	1,923	67
Costs and operating expenses:			
Cost of product revenue	465	457	8
Research and development	36,915	30,880	6,035
Selling and marketing	4,942	17,000	(12,058)
General and administrative	18,786	15,509	3,277
Total costs and operating expenses	61,108	63,846	(2,738)
Loss from operations	(59,118)	(61,923)	2,805
Other income (expense):			
Interest income	879	424	455
Interest expense	(1,739)	(1,892)	153
Other income (expense), net	—	5	(5)
Total other expense, net	(860)	(1,463)	603
Net loss	\$(59,978)	\$(63,386)	\$ 3,408

### Revenue

We generated \$2.0 and \$1.9 million of product revenue during the years ended December 31, 2018 and December 31, 2017, respectively, from sales of our ReSure Sealant product. The increase in revenue is related to an increase in the total number of units shipped in 2018.

### Research and Development Expenses

	Year Ended December 31,		Increase (Decrease)
	2018	2017	
(in thousands)			
Direct research and development expenses by program:			
ReSure Sealant	\$ 189	\$ 126	\$ 63
DEXTENZA for post-surgical ocular pain and inflammation	1,085	1,319	(234)
DEXTENZA for allergic conjunctivitis	20	621	(601)
DEXTENZA for dry eye disease	—	6	(6)
OTX-TP for glaucoma and ocular hypertension	5,305	5,288	17
Unallocated expenses:			
Personnel costs	17,706	15,211	2,495
All other costs	12,610	8,309	4,301
Total research and development expenses	<u>\$36,915</u>	<u>\$30,880</u>	<u>\$ 6,035</u>

Research and development expenses were \$36.9 million for the year ended December 31, 2018, compared to \$30.9 million for the year ended December 31, 2017. The increase of \$6.0 million was primarily due to an increase of \$6.8 million in unallocated expenses offset by decreases in clinical trial expenses of \$0.8 million. Clinical trial expenses decreased in the year ended December 31, 2018, compared to the year ended December 31, 2017, primarily due to the timing and number of clinical trials conducted for DEXTENZA for the treatment of post-surgical ocular pain and inflammation, allergic conjunctivitis and dry eye disease, partially offset by increases in clinical trial expenses related to OTX-TP for the treatment of glaucoma and ocular hypertension.

For the year ended December 31, 2018, we incurred \$6.4 million in direct research and development expenses for our intracanalicular insert product candidates, including \$1.1 million for DEXTENZA for the treatment of post-surgical ocular pain and inflammation, and \$5.3 million for our OTX-TP product candidate for the treatment of glaucoma and ocular hypertension which was in Phase 3 clinical trials. In comparison, for the year ended December 31, 2017, we incurred \$7.2 million in direct research and development expenses for our intracanalicular insert product candidates, including \$5.3 million for clinical trials of OTX-TP for glaucoma and ocular hypertension which was in Phase 3 clinical trials, \$0.6 million for DEXTENZA for the treatment of allergic conjunctivitis which was in Phase 3 clinical trials and \$1.3 million for DEXTENZA for ocular pain and inflammation following cataract surgery which was in Phase 3 clinical trials. Unallocated research and development costs increased \$6.8 million for the year ended December 31, 2018, compared to the year ended December 31, 2017 primarily due to an increase in unallocated personnel costs of \$2.5 million, relating to an increase of \$2.5 million from additional hiring primarily in our clinical, regulatory and quality department, \$2.1 million increase in professional services, and an increase in facility related costs of \$1.8 million.

### Selling and Marketing Expenses

	Year Ended December 31,		Increase (Decrease)
	2018	2017	
(in thousands)			
Personnel related (including stock-based compensation)	\$ 1,732	\$ 5,715	\$ (3,983)
Professional fees	2,563	10,296	(7,733)
Facility related and other	647	989	(342)
Total selling and marketing expenses	<u>\$ 4,942</u>	<u>\$17,000</u>	<u>\$(12,058)</u>

Selling and marketing expenses were \$4.9 million for the year ended December 31, 2018, compared to \$17.0 million for the year ended December 31, 2017. The decrease of \$12.1 million was primarily due to a decrease of \$4.0 million in personnel costs, a decrease of \$7.7 million in professional fees due to decreased spending on external costs and \$0.3 million in facility-related and other costs. The decrease overall was driven by a delay in the anticipated 2017 launch of DEXTENZA that is now projected to take place in the middle of 2019.

We therefore expect our selling and marketing expenses to increase in 2019 and beyond, due to the approval of DEXTENZA as we support the commercial launch. In August 2017, we reorganized our DEXTENZA commercial plans and realized savings in operating expenses, including reduced personnel costs, as a result of streamlining headcount, as part of an initiative to enhance operations and reduce expenses.

#### General and Administrative Expenses

	Year Ended December 31,		Increase (Decrease)
	2018	2017	
	(in thousands)		
Personnel related (including stock-based compensation)	\$ 8,367	\$ 8,353	\$ 14
Professional fees	8,761	5,463	3,298
Facility related and other	1,658	1,693	(35)
Total general and administrative expenses	<u>\$18,786</u>	<u>\$15,509</u>	<u>\$ 3,277</u>

General and administrative expenses were \$18.8 million for the year ended December 31, 2018, compared to \$15.5 million for the year ended December 31, 2017. The increase of \$3.3 million was primarily due to an increase of \$3.3 million in professional fees related to our defense in legal proceedings.

#### Other Income (Expense), Net

Other expense, net was \$0.9 million for the year ended December 31, 2018, compared to \$1.5 million for the year ended December 31, 2017.

#### Comparison of the Years Ended December 31, 2017 and December 31, 2016

The following table summarizes our results of operations for the years ended December 31, 2017 and 2016:

	Year Ended December 31,		Increase (Decrease)
	2017	2016	
	(in thousands)		
Revenue:			
Product revenue	\$ 1,923	\$ 1,845	\$ 78
Collaboration revenue	—	42	(42)
Total revenue	<u>1,923</u>	<u>1,887</u>	<u>36</u>
Costs and operating expenses:			
Cost of product revenue	457	443	14
Research and development	30,880	27,065	3,815
Selling and marketing	17,000	6,701	10,299
General and administrative	15,509	11,004	4,505
Total costs and operating expenses	<u>63,846</u>	<u>45,213</u>	<u>18,633</u>
Loss from operations	<u>(61,923)</u>	<u>(43,326)</u>	<u>(18,597)</u>
Other income (expense):			
Interest income	424	304	120
Interest expense	(1,892)	(1,680)	(212)
Other income (expense), net	5	(1)	6
Total other expense, net	<u>(1,463)</u>	<u>(1,377)</u>	<u>(86)</u>
Net loss	<u>\$ (63,386)</u>	<u>\$ (44,703)</u>	<u>\$ (18,683)</u>

#### Revenue

We generated \$1.9 and \$1.8 million of product revenue during the years ended December 31, 2017 and December 31, 2016, respectively, from sales of our ReSure Sealant product. The increase in revenue is related to an increase in the total number of units shipped in 2017. We generated \$42,000 of revenue from our collaboration agreements in 2016.

### Research and Development Expenses

	<b>Year Ended December 31,</b>		<b>Increase (Decrease)</b>
	<b>2017</b>	<b>2016</b>	
	(in thousands)		
Direct research and development expenses by program:			
ReSure Sealant	\$ 126	\$ 236	\$ (110)
DEXTENZA for post-surgical ocular pain and inflammation	1,319	2,686	(1,367)
DEXTENZA for allergic conjunctivitis	621	2,815	(2,194)
DEXTENZA for dry eye disease	6	101	(95)
OTX-TP for glaucoma and ocular hypertension	5,288	1,941	3,347
Unallocated expenses:			
Personnel costs	15,211	11,630	3,581
All other costs	8,309	7,656	653
Total research and development expenses	<u>\$30,880</u>	<u>\$27,065</u>	<u>\$ 3,815</u>

Research and development expenses were \$30.9 million for the year ended December 31, 2017, compared to \$27.1 million for the year ended December 31, 2016. The increase of \$3.8 million was primarily due to an increase of \$4.2 million in unallocated expenses offset by decreases in clinical trial expenses of \$0.3 million and expenses related to ReSure Sealant of \$0.1 million. Clinical trial and regulatory expenses decreased in the year ended December 31, 2017, compared to the year ended December 31, 2016, primarily due to the timing and number of clinical trials being conducted for DEXTENZA for the treatment of post-surgical ocular pain and inflammation, allergic conjunctivitis and dry eye disease, partially offset by increases in clinical trial expenses related to OTX-TP for the treatment of glaucoma and ocular hypertension.

For the year ended December 31, 2017, we incurred \$7.2 million in direct research and development expenses for our intracanalicular insert product candidates, including \$1.3 million for DEXTENZA for the treatment of post-surgical ocular pain and inflammation which was in Phase 3 clinical trials, \$0.6 million for DEXTENZA for the treatment of allergic conjunctivitis which was in Phase 3 clinical trials, and \$5.3 million for our OTX-TP product candidate for the treatment of glaucoma and ocular hypertension which was in Phase 3 clinical trials. In comparison, for the year ended December 31, 2016, we incurred \$7.6 million in direct research and development expenses for our intracanalicular insert product candidates, including \$2.0 million for clinical trials of OTX-TP for glaucoma and ocular hypertension which was in Phase 3 clinical trials, \$2.8 million for DEXTENZA for the treatment of allergic conjunctivitis which was in Phase 3 clinical trials and \$2.7 million for DEXTENZA for ocular pain and inflammation following cataract surgery which was in Phase 3 clinical trials and \$0.1 million for DEXTENZA for the treatment of dry eye disease which was in Phase 2 clinical trials. Unallocated research and development costs increased \$4.2 million for the year ended December 31, 2017, compared to the year ended December 31, 2016 primarily due to an increase in unallocated personnel costs of \$3.6 million, relating to an increase of \$2.2 million from additional hiring primarily in our clinical, regulatory and quality department, \$0.7 million increase in restructuring and other costs, and an increase in stock-based compensation expense of \$0.7 million.

### Selling and Marketing Expenses

	<b>Year Ended December 31,</b>		<b>Increase (Decrease)</b>
	<b>2017</b>	<b>2016</b>	
	(in thousands)		
Personnel related (including stock-based compensation)	\$ 5,715	\$ 2,580	\$ 3,135
Professional fees	10,296	2,993	7,303
Facility related and other	989	1,128	(139)
Total selling and marketing expenses	<u>\$17,000</u>	<u>\$ 6,701</u>	<u>\$10,299</u>

Selling and marketing expenses were \$17.0 million for the year ended December 31, 2017, compared to \$6.7 million for the year ended December 31, 2016. The increase of \$10.3 million was primarily due to an increase of \$1.7 million in personnel costs and increase of \$1.4 million of severance related costs, an increase of \$7.3 million in professional fees due to increased spending on external costs offset by a decrease of \$0.1 million in facility-related and other costs. The increase in consulting expenses was primarily due to marketing activities that were undertaken in

preparation for a potential launch of DEXTENZA for the treatment of post-surgical ocular pain subject to our obtaining FDA approval.

In August 2017, we reorganized our DEXTENZA commercial plans and expect to realize savings in operating expenses, including reduced personnel costs, as a result of streamlining headcount, as part of an initiative to enhance operations and reduce expenses.

#### *General and Administrative Expenses*

	<b>Year Ended</b>		<b>Increase (Decrease)</b>
	<b>December 31,</b>		
	<b>2017</b>	<b>2016</b>	
	<b>(in thousands)</b>		
Personnel related (including stock-based compensation)	\$ 8,353	\$ 6,184	\$ 2,169
Professional fees	5,463	3,732	1,731
Facility related and other	1,693	1,088	605
Total general and administrative expenses	<u>\$15,509</u>	<u>\$11,004</u>	<u>\$ 4,505</u>

General and administrative expenses were \$15.5 million for the year ended December 31, 2017, compared to \$11.0 million for the year ended December 31, 2016. The increase of \$4.5 million was due to a \$2.2 million increase in personnel related costs and an increase of \$1.7 million in professional fees, and an increase of \$0.6 million in facility-related and other costs. Our personnel related costs increased primarily due \$1.2 million relating to additional hiring, \$0.4 million of severance related costs related to the termination our former chief operating officer, and an increase in stock compensation expense of \$0.5 million. Professional fees increased primarily due to an increase of \$0.7 million relating to recruiting and relocation fees, \$0.6 million in legal costs and \$0.4 million related to consulting fees.

#### *Other Income (Expense), Net*

Other expense, net was \$1.5 million for the year ended December 31, 2017, compared to \$1.4 million for the year ended December 31, 2016.

#### **Liquidity and Capital Resources**

Since inception, we have incurred significant operating losses. Our net losses were \$60.0 million, \$63.4 million and \$44.7 million for the years ended December 31, 2018, 2017 and 2016, respectively. As of December 31, 2018, we had an accumulated deficit of \$297.2 million.

We have generated limited revenue to date. In the first quarter of 2014, we began recognizing revenue from sales of ReSure Sealant. All of our local programmed-release drug delivery products are in various phases of clinical and preclinical development. We do not expect sales of ReSure Sealant to generate revenue that is sufficient for us to achieve profitability. Instead, our ability to generate product revenue sufficient to achieve profitability will depend heavily on our obtaining marketing approval for and commercializing products with greater market potential, including DEXTENZA and OTX-TP.

Through December 31, 2018, we have financed our operations primarily through private placements of our preferred stock, public offerings of our common stock and borrowings under credit facilities. In July 2014, we completed our IPO, and in August 2014 the underwriters in our IPO exercised their over-allotment option in full. We received total net proceeds of approximately \$66.4 million from the issuance and sale of 5,750,000 shares of common stock, including in connection with the exercise by the underwriters of their over-allotment option, after deducting underwriting discounts and offering costs. In June 2015, we completed a follow-on offering of our common stock at a public offering price of \$22.00 per share. The offering consisted of 4,600,000 shares of common stock, of which 3,200,000 shares were issued and sold by us and 1,400,000 shares were sold by certain stockholders, including those shares sold in connection with the exercise by the underwriters of their option to purchase additional shares. We received net proceeds from the follow-on offering of approximately \$65.6 million after deducting underwriting discounts and commissions, and offering expenses. In November 2016, we entered into the 2016 Sales Agreement with Cantor, under which we could offer and sell our common stock having aggregate proceeds of up to \$40.0 million from time to time. Through February 25, 2019, we have 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, commission and other offering expenses. On February 28, 2019, pursuant to the 2016 Sales Agreement, we delivered a termination notice to Cantor, terminating the

2016 Sales Agreement. In January 2017, we completed a follow-on offering of our common stock at a public offering price of \$7.00 per share. The offering consisted of 3,571,429 shares of common stock sold by us. We received net proceeds from the follow-on offering of approximately \$23.3 million after deducting underwriting discounts, commissions and expenses. In January 2018, we completed a follow-on offering of our common stock at a public offering price of \$5.00 per share. The offering consisted of 7,475,000 shares of common stock sold by us, including those shares sold in connection with the exercise by the underwriter of its option to purchase additional shares. We received net proceeds from the follow-on offering of approximately \$35.1 million after deducting underwriting discounts and commissions.

As of December 31, 2018, we had cash and cash equivalents of \$54.1 million. In March 2019, we completed a private placement of senior subordinated convertible notes and received net proceeds from the offering of \$37.1 million.

As of December 31, 2018, we had outstanding debt of \$25.0 million. In April 2014, we borrowed \$15.0 million in aggregate principal amount under a new 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 our credit facility to increase the aggregate principal amount to \$15.6 million, extend the interest-only payment period through December 2016, and extend the maturity date to December 1, 2019. The outstanding borrowings under this facility bear interest at an annual rate equal to 8.25%. In March 2017, we amended the credit facility to increase the total indebtedness to \$18.0 million. The interest-only payment period was extended through February 1, 2018. In December 2018, we amended the credit facility to increase the total indebtedness to \$25.0 million. The interest-only payment period was extended through December 2020. In March 2019, we also issued \$37.5 million aggregate principal amount of senior subordinated convertible notes that mature in 2026. See “—Contractual Obligations and Commitments” for additional information.

### Cash Flows

As of December 31, 2018, we had cash and cash equivalents of \$54.1 million and outstanding debt of \$25.0 million. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation. Based on our current plans and forecasted expenses, we believe that our existing cash and cash equivalents, as of December 31, 2018, together with the net proceeds from our private placement of convertible notes, without giving effect to any potential payment under our Collaboration Agreement with Regeneron, will enable us to fund our operating expenses, debt service obligations and capital expenditure requirements into early 2020. 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. These factors, and the factors described above, continue to raise substantial doubt about our ability to continue as a going concern.

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

	<u>Year Ended December 31,</u>		
	<u>2018</u>	<u>2017</u>	<u>2016</u>
	(in thousands)		
Cash used in operating activities	\$(49,227)	\$(50,473)	\$(34,001)
Cash (used in) provided by investing activities	(1,889)	27,067	35,568
Cash provided by financing activities	68,640	32,008	585
Net increase in cash and cash equivalents	<u>\$ 17,524</u>	<u>\$ 8,602</u>	<u>\$ 2,152</u>

*Operating activities.* Net cash used in operating activities was \$49.2 million for the year ended December 31, 2018, primarily resulting from our net loss of \$60.0 million, partially offset by non-cash charges of \$10.2 million and cash provided by changes in our operating assets and liabilities of \$0.6 million. Our net loss was primarily attributed to research and development activities and our general and administrative expenses partially offset by \$2.0 million of revenue in the period. Our net non-cash charges during the year ended December 31, 2018 primarily consisted of \$7.5 million of stock-based compensation expense and \$2.3 million of depreciation expense. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2018 consisted primarily of a \$1.7 million increase in accrued expenses and deferred rent and a \$0.8 million decrease in accounts payable, which was due to the timing of vendor invoicing and payments.

Net cash used in operating activities was \$50.5 million for the year ended December 31, 2017, primarily resulting from our net loss of \$63.4 million, partially offset by non-cash charges of \$9.4 million and cash provided by changes in our operating assets and liabilities of \$3.6 million. Our net loss was primarily attributed to research and development activities and our general and administrative expenses partially offset by \$1.9 million of revenue in the period. Our net non-cash charges during the year ended December 31, 2017 primarily consisted of \$7.3 million of stock-based compensation expense and \$1.6 million of depreciation expense. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2017 consisted primarily of a \$2.6 million increase in accrued expenses and deferred rent and a \$0.9 million increase in accounts payable, which was due to the timing of vendor invoicing and payments.

Net cash used in operating activities was \$34.0 million for the year ended December 31, 2016, primarily resulting from our net loss of \$44.7 million, partially offset by non-cash charges of \$7.2 million and cash provided by changes in our operating assets and liabilities of \$2.1 million. Our net loss was primarily attributed to research and development activities and our general and administrative expenses partially offset by \$1.9 million of revenue in the period. Our net non-cash charges during the year ended December 31, 2016 primarily consisted of \$6.0 million of stock-based compensation expense and \$0.9 million of depreciation expense. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2016 consisted primarily of a \$1.4 million increase in accrued expenses and deferred rent, a \$0.9 million decrease in prepaid expenses and other current assets, and a \$0.2 million increase in accounts payable, which was due to the timing of vendor invoicing and payments.

*Investing activities.* Net cash used in investing activities was \$1.9 million for the year ended December 31, 2018, consisting of cash used to purchase property and equipment of \$1.9 million. Net cash provided by investing activities was \$27.1 million for the year ended December 31, 2017 consisted of maturities of marketable securities of \$38.2 million offset by cash used to purchase property and equipment of \$8.3 million and cash used to purchase marketable securities of \$3.0 million. Net cash provided by investing activities for the year ended December 31, 2016 consisted of maturities of marketable securities of \$80.7 million offset by cash used to purchase property and equipment of \$1.9 million and cash used to purchase marketable securities of \$41.7 million.

*Financing activities.* Net cash provided by financing activities for 2018 was \$68.6 million and consisted primarily of proceeds from our follow-on offering in January 2018 of \$34.7 and the 2016 Sales Agreement of \$26.9 million, net of underwriting discounts and other offering expenses, \$6.4 million (net) in borrowings under our amended credit facility, proceeds from the exercise of common stock options of \$0.4 million; and proceeds from issuance of common stock pursuant to our employee stock purchase plan of \$0.3 million. Net cash provided by financing activities for 2017 was \$32.0 million and consisted primarily of proceeds from our follow-on offering in January 2017 of \$23.3 and the 2016 Sales Agreement of \$5.9 million, net of underwriting discounts and other offering expenses, \$2.4 million (net) in borrowings under our amended credit facility, proceeds from the exercise of common stock options of \$0.7 million; and proceeds from issuance of common stock pursuant to our employee stock purchase plan of \$0.3 million partially offset by payments of \$0.6 million for insurance costs financed by a third party. Net cash provided by financing activities for 2016 was \$0.6 million and consisted primarily of proceeds of \$0.6 million, net of underwriting discounts and other offering expenses, related to the 2016 Sales Agreement, proceeds from the exercise of common stock options of \$0.2 million; and proceeds from issuance of common stock pursuant to our employee stock purchase plan of \$0.3 million partially offset by payments of \$0.5 million for insurance costs financed by a third party.

### ***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 focused on the potential launch of our product candidates, subject to receiving FDA approval.

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

- commercially launch DEXTENZA in the United States;
- continue to develop and expand our sales, marketing and distribution capabilities for DEXTENZA and any of our product candidates;

- continue to pursue the clinical development of our most advanced intracanalicular insert product candidates, OTX-TP and DEXTENZA in additional indications;
- continue clinical trials of our product candidates OTX-TIC and OTX-TKI;
- 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;
- 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 back-of-the-eye program and glaucoma intracameral implant program 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 the expected growth in personnel;
- renovate our new facility 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, we believe that our existing cash and cash equivalents, as of December 31, 2018, together with the net proceeds from our private placement of convertible notes, without giving effect to any potential payment under our Collaboration Agreement with Regeneron, will enable us to fund our operating expenses, debt service obligations and capital expenditure requirements into early 2020. 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 successfully 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 expected growth in personnel;
- the progress, costs and outcome of the clinical trials of our extended-delivery drug delivery product candidates, in particular OTX-TP and DEXTENZA for additional indications;
- the progress and status of our collaboration with Regeneron, including any development costs for which we reimburse Regeneron, the potential exercise by Regeneron of its option for a license for the development and potential commercialization of products containing our extended-delivery hydrogel formulation in combination with Regeneron's large molecule VEGF-targeting compounds, and our potential receipt of future milestone payments from Regeneron;
- the costs of advancing our internal development efforts for the back-of-the-eye small molecule TKI program through the remaining preclinical steps and potentially into an initial clinical trial;
- the scope, progress, costs and outcome of preclinical development and clinical trials of our other product candidates;
- the extent of our debt service obligations;
- the amounts we receive, if any, from Regeneron for option exercise, development, regulatory and sales milestones and royalty payments under our collaboration;
- 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, including the current lawsuits described under "Item 3 — Legal 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 and marketing and distribution arrangements. We do not have any committed external source of funds other than amounts we may receive from Regeneron for potential option exercise, development, regulatory and sales milestones and royalties under our collaboration. 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 facility, the pledge of our assets as collateral and the negative pledge of intellectual property 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 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. 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.

As discussed in Note 1 of the Notes to the Consolidated Financial Statements under Accounting Standards Update, or ASU, 2014-15, Presentation of Financial Statements—Going Concern (Subtopic 205-40), or, ASC 205-40, we have the responsibility to evaluate whether conditions or events raise substantial doubt about our ability to meet our future financial obligations as they become due within one year after the date the financial statements are issued. Under ASC 205-40, this evaluation initially cannot take into consideration the potential mitigating effects of plans that have not been fully implemented as of the date the financial statements are issued. Since we currently anticipate that our existing capital resources, together with the net proceeds from our private placement of convertible notes, without giving effect to any potential payment under our Collaboration Agreement with Regeneron, will enable us to meet our planned operational expenses, debt service obligations, and capital expenditures, based on our current operating plans, into early 2020, we have determined that this cash runway of less than 12 months along with our accumulated deficit, history of losses, and future expected losses meet the ASC 205-40 standard for raising substantial doubt about our ability to continue as a going concern within one year of the issuance date of these financial statements. While we have plans in place to mitigate this risk, which primarily consist of raising additional capital through a combination of equity or debt financings, and, depending on the availability and level of additional financings, potentially new collaborations and reducing cash expenditures, there is no guarantee that we will be successful in these mitigation efforts.

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, 2018, we had federal net operating loss carryforwards of \$190.6 million, which begin to expire in 2026, and state net operating loss carryforwards of \$161.8 million, which begin to expire in 2026. As of December 31, 2018, we also had federal research and development tax credit carryforwards of \$7.0 million and state research and development tax credit carryforwards \$3.6 million, 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

The following table summarizes our contractual obligations at December 31, 2018 and the effects such obligations are expected to have on our liquidity and cash flow in future periods:

	Total	Less Than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 Years
	(in thousands)				
Operating lease commitments	\$ 14,434	\$ 1,808	\$ 3,736	\$ 3,666	\$ 5,224
Purchase commitments	3,504	1,930	1,444	130	—
Manufacturing commitments	66	66	—	—	—
Debt obligations including interest	34,638	2,474	12,908	19,256	—
<b>Total</b>	<b>\$ 52,642</b>	<b>\$ 6,278</b>	<b>\$18,088</b>	<b>\$23,052</b>	<b>\$ 5,224</b>

In the table above, we set forth our enforceable and legally binding obligations and future commitments at December 31, 2018, 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, 2018. 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 obligations we will actually pay in future periods may vary from those reflected in the table.

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 and July 2027.

In June 2016, we entered into a lease agreement for approximately 70,712 square feet of general office, research and development and manufacturing space. The lease term commenced on February 1, 2017 and expires on July 31, 2027. No base rent was due under the lease until August 1, 2017. The initial annual base rent is approximately \$1.2 million and will increase annually beginning on February 1 of each year. We are obligated to pay all real estate taxes

and costs related to the premises, including costs of operations, maintenance, repair, and replacement and management of the new leased premises. We posted a customary letter of credit in the amount of \$1.5 million as a security deposit. We relocated our corporate headquarters to the new leased premises in June 2017 and are evaluating the potential relocation of our manufacturing operations to the new leased premises. The lease agreement allowed for a construction allowance not to exceed approximately \$2.8 million to be applied to the total construction costs of the new leased premises. The construction allowance had to be used before December 31, 2017, or it would be deemed forfeited with no further obligation by the landlord of the new leased premises. As of December 31, 2017, we billed the landlord for \$2.7 million and subsequently, we have received payments of \$2.7 million from the landlord. We forfeited \$0.1 million under the construction allowance.

On October 10, 2017, we entered into an amendment to the lease agreement for our laboratory and manufacturing space located at 34 Crosby Drive and 36 Crosby Drive, each in Bedford, Massachusetts, which we refer to as the Second Amendment. The Second Amendment extends the term of our lease for 36 Crosby Drive from June 30, 2018 to July 31, 2023. Further, the Second Amendment acknowledges that we have previously vacated and surrendered, and the lease has expired with regards to 34 Crosby Drive, reducing the total laboratory and manufacturing space subject to the lease to 20,445 square feet. Accordingly, the Second Amendment reduces the required security deposit under the lease from \$0.2 million to \$0.1 million. Under the Second Amendment, the annual base rent for 36 Crosby Drive shall be approximately \$0.5 million until June 30, 2018, shall be \$0 from July 1, 2018 to July 31, 2018, and shall be approximately \$0.5 million from August 1, 2018 to July 31, 2019. The annual base rent shall increase annually thereafter. The Second Amendment also provides us a one-time option to terminate the Lease on July 31, 2021, upon the delivery to the landlord on or before July 31, 2020, of a termination notice and the payment to the landlord of a termination fee of approximately \$0.3 million.

Purchase commitments represent non-cancelable contractual commitments associated with certain clinical trial activities with our CROs.

Manufacturing commitments generally provide for termination on notice, and therefore are cancelable contracts but are contracts that we are likely to continue, regardless of the fact that they are cancelable.

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 in the table of contractual obligations and commitments.

In April 2014, we entered into a credit facility with Silicon Valley Bank and MidCap Financial SBIC, LP, pursuant to which we were able to borrow an aggregate principal amount of up to \$20.0 million, of which we borrowed \$15.0 million. We did not borrow the remaining \$5.0 million, and this amount is no longer available to us. The credit facility carries a fixed annual interest rate of 8.25% on outstanding borrowings. In April 2014, we issued the lenders warrants to purchase 100,000 shares of our Series D-1 redeemable convertible preferred stock with an exercise price of \$3.00 per share. Upon the closing of our IPO in July 2014, the preferred stock warrants became warrants to purchase an aggregate of 37,878 shares of our common stock with an exercise price of \$7.92 per share.

In December 2015, we amended the credit facility to increase the aggregate principal amount to \$15.6 million to capitalize certain accrued interest. The amended facility provides for monthly, interest-only payments on outstanding borrowings through December 2016. Thereafter, we were required to pay thirty-six consecutive, equal monthly installments of principal and interest through December 1, 2019. In March 2017, we further amended the credit facility to \$18.0 million of borrowings. The interest-only payment period was extended through February 1, 2018. There are no financial covenants associated with the credit facility. In December 2018, we further amended the credit facility to increase the aggregate principal amount borrowed to \$25.0 million. The interest-only payments was extended through December 2020. 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. Under the December 2018 amendment, we are required to maintain a minimum of \$5.0 million of cash and/or cash equivalents on hand as a financial covenant to the borrowing arrangement. There are no other financial covenants associated with the amended facility; however, there are negative covenants restricting our activities, including limitations on dispositions, mergers or acquisitions; incurring indebtedness, liens or encumbrances; paying dividends; making certain investments; and engaging in certain other business transactions. The obligations under the amended facility are subject to acceleration upon the occurrence of

specified events of default, including a material adverse change in our business, operations or financial or other condition. The debt is collateralized by a first-priority lien on all of our assets, including our intellectual property.

In connection with our entry into the Purchase Agreement, as described below, in February 2019, we further amended the credit facility to permit our issuance and sale of the Notes in March 2019. The February amendment added, among other provisions, a negative covenant restricting us from paying the holders of the Notes ahead in priority to the senior 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 also constituted an event of default under the credit facility.

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 that we entered into with Incept in January 2012. 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 covered by the licensed technology. Any sublicensee of ours 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 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 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.

In February 2019, we entered into a note purchase agreement, or the Purchase Agreement, with Cap 1 LLC, an affiliate of Summer Road LLC, or the Purchaser, to issue and sell to the Purchaser unsecured senior subordinated convertible notes, or the Notes, in the original aggregate principal amount of \$37.5 million. In accordance with the Purchase Agreement, each Note accrues interest at a rate of 6% of its outstanding principal amount per annum, payable at maturity. The maturity date of each Note is March 1, 2026, unless earlier converted, repurchased or redeemed as described below.

Holders may, subject to certain conditions, convert all or part of the outstanding principal amount of their Notes into shares of 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 conversion rate for the Notes will initially be 153.8462 shares of our common stock per \$1,000 principal amount of the Notes, which is equivalent to an initial conversion price of approximately \$6.50 per share. The conversion rate is subject to adjustment in customary circumstances such as stock splits or similar changes 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 Note, we are obligated to make a cash payment to the holder of such Note for any interest accrued but unpaid on the principal amount converted. Upon the occurrence of a Corporate Transaction (as defined in the Notes), the holder of a Note is entitled, at such holder's option, to convert all of the outstanding principal amount of the Note in accordance with the foregoing and receive an additional, "make-whole" cash payment in accordance with a table set forth in each Note.

Upon the occurrence of a Corporate Transaction, each holder of a Note has the option to require us 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 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 Notes, on a pro rata basis, at an optional redemption price equal to 100% of the outstanding principal amount of the 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 Purchaser. The Purchase Agreement does not include any financial covenants. Our obligations under the Purchase Agreement and the 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.

### **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.

### **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, 2018, we had cash and cash equivalents of \$54.1 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-28 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, 2018. 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, 2018, 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 Rule 13a-15(f) or 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. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. 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, 2018. 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, 2018, our internal control over financial reporting was effective.

As an “emerging growth company,” as defined in the JOBS Act, our independent registered accounting firm is not required to issue an attestation report on the internal control over financial reporting.

### **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, 2018 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 2019 Annual Meeting of Stockholders and is incorporated in this Annual Report on Form 10-K by reference.

#### **Compliance with Section 16(a) of the Exchange Act**

The information required by this item will be set forth in our Proxy Statement for the 2019 Annual Meeting of Stockholders 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 2019 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 2019 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 2019 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 2019 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 2019 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 2019 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 2019 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:

	<u>Page</u>
<a href="#">Report of Independent Registered Public Accounting Firm</a>	F-2
<a href="#">Consolidated Balance Sheets</a>	F-3
<a href="#">Consolidated Statements of Operations and Comprehensive Loss</a>	F-4
<a href="#">Consolidated Statements of Changes in Stockholders' Equity</a>	F-5
<a href="#">Consolidated Statements of Cash Flows</a>	F-6
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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 our consolidated financial statements. 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			Exhibit Number	Filed Herewith
		Form	File Number	Date of Filing		
3.1	<a href="#">Restated Certificate of Incorporation of the Registrant</a>	8-K	001-36554	7/30/2014	3.1	
3.2	<a href="#">Amended and Restated Bylaws of the Registrant</a>	8-K	001-36554	7/30/2014	3.2	
4.1	<a href="#">Specimen Stock Certificate evidencing the shares of common stock</a>	S-1/A	333-196932	7/11/2014	4.1	
4.2	<a href="#">Registration Rights Agreement, dated as of March 1, 2019, by and among the Registrant and the Purchasers identified therein</a>					X
10.1+	<a href="#">2006 Stock Incentive Plan, as amended</a>	S-1	333-196932	6/20/2014	10.1	
10.2+	<a href="#">Form of Stock Option Agreement under 2006 Stock Incentive Plan</a>	S-1	333-196932	6/20/2014	10.2	
10.3+	<a href="#">Form of Restricted Stock Agreement under 2006 Stock Incentive Plan</a>	S-1	333-196932	6/20/2014	10.3	
10.4+	<a href="#">2014 Stock Incentive Plan</a>	S-1/A	333-196932	7/11/2014	10.4	
10.5+	<a href="#">Form of Incentive Stock Option Agreement under 2014 Stock Incentive Plan</a>	S-1/A	333-196932	7/11/2014	10.5	
10.6+	<a href="#">Form of Non-statutory Stock Option Agreement under 2014 Stock Incentive Plan</a>	S-1/A	333-196932	7/11/2014	10.6	
10.7+	<a href="#">Form of Restricted Stock Agreement under 2014 Stock Incentive Plan</a>	S-1/A	333-196932	7/11/2014	10.7	
10.8†	<a href="#">Amended and Restated License Agreement, dated January 27, 2012, between the Registrant and Incept LLC</a>	S-1	333-196932	6/20/2014	10.8	
10.9	<a href="#">Lease Agreement dated September 2, 2009, by and between the Registrant and RAR2-Crosby Corporate Center QRS, Inc., as amended.</a>	S-1	333-196932	6/20/2014	10.9	
10.10+	<a href="#">2014 Employee Stock Purchase Plan</a>	S-1/A	333-196932	7/11/2014	10.10	
10.11	<a href="#">Form of Indemnification Agreement by and between the Registrant and each of its directors and executive officers</a>	S-1	333-196932	6/20/2014	10.12	

Exhibit Number	Description of Exhibit	Incorporated by Reference			Filed Herewith
		Form	File Number	Date of Filing	
10.12+	<a href="#">Amended and Restated Employment Agreement, dated June 24, 2014, by and between the Registrant and Amarpreet S. Sawhney, Ph.D.</a>	S-1/A	333-196932	7/11/2014	10.13
10.13	<a href="#">Lease Agreement dated June 17, 2016 between the WS NF 15 Crosby Drive, LLC and the Registrant</a>	10-Q	001-36554	8/9/2016	10.1
10.14†	<a href="#">Collaboration, Option and License Agreement between the Registrant and Regeneron Pharmaceuticals, Inc. dated October 10, 2016</a>	10-Q	001-36554	11/9/2016	10.1
10.15	<a href="#">Controlled Equity Offering Sales Agreement, dated November 29, 2016, by and between the Registrant and Cantor Fitzgerald &amp; Co.</a>	8-K	001-36554	11/30/2016	1.1
10.16	<a href="#">Second Amended and Restated Credit and Security Agreement, dated March 7, 2017, by and among MidCap Financial Trust, the Registrant and the Lenders listed therein</a>	10-Q	001-36554	5/5/2017	10.1
10.17+	<a href="#">Amendment to Employment Agreement, by and between the Registrant and Amarpreet S. Sawhney, dated as of June 20, 2017</a>	8-K	001-36554	6/22/2017	10.1
10.18+	<a href="#">Employment Agreement, by and between the Registrant and Antony C. Mattessich, dated as of June 20, 2017</a>	8-K	001-36554	6/22/2017	10.2
10.19+	<a href="#">Non-Statutory Stock Option Agreement, by and between the Registrant and Antony C. Mattessich dated as of June 20, 2017</a>	8-K	001-36554	6/22/2017	10.3
10.20+	<a href="#">Transition, Separation and Release of Claims Agreement by and between the Registrant and Eric Ankerud, dated as of July 31, 2017</a>	8-K	001-36554	8/3/2017	10.1
10.21	<a href="#">Consulting Agreement by and between the Registrant and Anchor Biotech Consulting, LLC dated as of July 31, 2017</a>	8-K	001-36554	8/3/2017	10.2
10.22+	<a href="#">Employment Agreement, by and between the Registrant and Donald Notman, dated as of September 25, 2017</a>	8-K	001-36554	9/25/2017	10.1

Exhibit Number	Description of Exhibit	Incorporated by Reference			Filed Herewith
		Form	File Number	Date of Filing	
10.23	<a href="#">Second Amendment to Lease, by and between the Registrant and CCC Investors LLC, dated October 10, 2017</a>	8-K	001-36554	10/16/2017	10.1
10.24+	<a href="#">Transition, Separation and Release of Claims Agreement by and between the Registrant and James Fortune, dated as of October 13, 2017</a>	8-K	001-36554	10/13/2017	10.1
10.25+	<a href="#">Employment Agreement, by and between the Registrant and Daniel Bollag, dated as of July 31, 2017</a>	10-K	001-36554	3/8/2018	10.29
10.26+	<a href="#">Employment Agreement, by and between the Registrant and Michael Goldstein, dated as of September 25, 2017</a>	10-K	001-36554	3/8/2018	10.30
10.27+	<a href="#">Employment Agreement, by and between the Registrant and Kevin Hanley, dated as of January 5, 2018</a>	10-K	001-36554	3/8/2018	10.31
10.28+	<a href="#">Second Amendment to Employment Agreement, by and between the Registrant and Amarpreet S. Sawhney, dated August 6, 2018</a>	10-Q	001-36554	8/7/2018	10.1
10.29†	<a href="#">Second Amended and Restated License Agreement, dated September 13, 2018, by and between the Registrant and Incept LLC</a>	8-K	001-36554	9/19/2018	10.1
10.30	<a href="#">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</a>	8-K	001-36554	12/28/2018	10.1
10.31	<a href="#">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</a>	8-K	001-36554	2/22/2019	10.3
10.32	<a href="#">Subordination Agreement, dated as of February 21, 2019, by and among the Registrant, MidCap Financial Trust, as administrative agent, and the Lenders listed therein</a>	8-K	001-36554	2/22/2019	10.4

Exhibit Number	Description of Exhibit	Incorporated by Reference			Filed Herewith
		Form	File Number	Date of Filing	
10.33	<a href="#">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</a>	8-K	001-36554	2/22/2019	10.1
23.1	<a href="#">Consent of PricewaterhouseCoopers LLP</a>				X
31.1	<a href="#">Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended</a>				X
31.2	<a href="#">Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended</a>				X
32.1	<a href="#">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</a>				X
32.2	<a href="#">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</a>				X
101.INS	XBRL Instance Document				X
101.SCH	XBRL Taxonomy Extension Schema Document				X
101.CAL	XBRL Taxonomy Calculation Linkbase Document				X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document				X
101.LAB	XBRL Taxonomy Label Linkbase Document				X
101.PRE	XBRL Taxonomy Presentation Linkbase Document				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.

## 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 7, 2019

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.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Antony Mattessich</u> Antony Mattessich	President and Chief Executive Officer (Principal Executive Officer)	March 7, 2019
<u>/s/ Donald Notman</u> Donald Notman	Chief Financial Officer (Principal Financial and Accounting Officer)	March 7, 2019
<u>/s/ Amarpreet Sawhney, Ph.D.</u> Amarpreet Sawhney, Ph.D	Chairman of the Board	March 7, 2019
<u>/s/ Jaswinder Chadha</u> Jaswinder Chadha	Director	March 7, 2019
<u>/s/ Jeffrey S. Heier, M.D.</u> Jeffrey S. Heier, M.D.	Director	March 7, 2019
<u>/s/ Richard L. Lindstrom, M.D.</u> Richard L. Lindstrom, M.D.	Director	March 7, 2019
<u>/s/ William James O'Shea</u> William James O'Shea	Director	March 7, 2019
<u>/s/ Bruce A. Peacock</u> Bruce A. Peacock	Director	March 7, 2019
<u>/s/ Charles Warden</u> Charles Warden	Director	March 7, 2019

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**OCULAR THERAPEUTIX, INC.**

**INDEX TO CONSOLIDATED FINANCIAL STATEMENTS**

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<a href="#">Consolidated Balance Sheets</a>	F-3
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## 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, 2018 and 2017, and the related consolidated statements of operations and comprehensive loss, of changes in stockholders’ equity and of cash flows for each of the three years in the period ended December 31, 2018, 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, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018 in conformity with accounting principles generally accepted in the United States of America.

### ***Substantial Doubt About the Company’s Ability to Continue as a Going Concern***

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has incurred losses and negative cash flows from operations since its inception, which raise substantial doubt about its ability to continue as a going concern. Management’s plans in regard to these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

### ***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.

/s/ PricewaterhouseCoopers LLP  
Boston, Massachusetts  
March 7, 2019

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, 2018	December 31, 2017
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 54,062	\$ 41,538
Accounts receivable	201	226
Inventory	217	122
Prepaid expenses and other current assets	1,713	1,453
Total current assets	56,193	43,339
Property and equipment, net	10,236	10,478
Restricted cash	6,614	1,614
Total assets	<u>\$ 73,043</u>	<u>\$ 55,431</u>
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable	\$ 2,965	\$ 3,571
Accrued expenses and deferred rent	6,194	4,310
Notes payable, net of discount, current	—	5,545
Total current liabilities	9,159	13,426
Deferred rent, long-term	3,221	3,387
Notes payable, net of discount, long-term	24,788	12,471
Total liabilities	<u>37,168</u>	<u>29,284</u>
Commitments and contingencies (Note 13)		
Stockholders' equity:		
Preferred stock, \$0.0001 par value; 5,000,000 shares authorized and no shares issued or outstanding at December 31, 2018 and December 31, 2017, respectively	—	—
Common stock, \$0.0001 par value; 100,000,000 shares authorized and 41,518,091 and 29,658,202 shares issued and outstanding at December 31, 2018 and December 31, 2017	4	3
Additional paid-in capital	333,114	263,409
Accumulated deficit	<u>(297,243)</u>	<u>(237,265)</u>
Total stockholders' equity	35,875	26,147
Total liabilities and stockholders' equity	<u>\$ 73,043</u>	<u>\$ 55,431</u>

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,		
	2018	2017	2016
<b>Revenue:</b>			
Product revenue	\$ 1,990	\$ 1,923	\$ 1,845
Collaboration revenue	—	—	42
Total revenue	1,990	1,923	1,887
<b>Costs and operating expenses:</b>			
Cost of product revenue	465	457	443
Research and development	36,915	30,880	27,065
Selling and marketing	4,942	17,000	6,701
General and administrative	18,786	15,509	11,004
Total costs and operating expenses	61,108	63,846	45,213
Loss from operations	(59,118)	(61,923)	(43,326)
<b>Other income (expense):</b>			
Interest income	879	424	304
Interest expense	(1,739)	(1,892)	(1,680)
Other income (expense), net	—	5	(1)
Total other expense, net	(860)	(1,463)	(1,377)
Net loss	\$ (59,978)	\$ (63,386)	\$ (44,703)
Net loss per share, basic and diluted	\$ (1.57)	\$ (2.20)	\$ (1.80)
Weighted average common shares outstanding, basic and diluted	38,115,142	28,818,196	24,816,348
<b>Comprehensive loss:</b>			
Net loss	\$ (59,978)	\$ (63,386)	\$ (44,703)
<b>Other comprehensive loss:</b>			
Unrealized gain on marketable securities	—	5	63
Total other comprehensive income	—	5	63
Total comprehensive loss	\$ (59,978)	\$ (63,381)	\$ (44,640)

The accompanying notes are an integral part of these consolidated financial statements.

**OCULAR THERAPEUTIX, INC.**

**CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY**

(In thousands, except share data)

	Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Par Value				
<b>Balances at December 31, 2015</b>	—	\$ —	24,750,281	\$ 2	\$ 218,830	\$ (129,176)	\$ (68)	\$ 89,588
Issuance of common stock upon exercise of stock options	—	—	105,114	—	199	—	—	199
Issuance of common stock in connection with employee stock purchase plan	—	—	66,628	—	278	—	—	278
Issuance of common stock upon public offering, net of issuance costs	—	—	102,077	1	626	—	—	627
Unrealized loss on marketable securities	—	—	—	—	—	—	63	63
Stock-based compensation expense	—	—	—	—	5,956	—	—	5,956
Net loss	—	—	—	—	—	(44,703)	—	(44,703)
<b>Balances at December 31, 2016</b>	—	—	25,024,100	3	225,889	(173,879)	(5)	52,008
Issuance of common stock upon exercise of stock options	—	—	220,520	—	685	—	—	685
Issuance of common stock in connection with employee stock purchase plan	—	—	53,662	—	276	—	—	276
Issuance of common stock upon public offering, net of issuance costs	—	—	4,359,920	—	29,238	—	—	29,238
Unrealized gain on marketable securities	—	—	—	—	—	—	5	5
Stock-based compensation expense	—	—	—	—	7,321	—	—	7,321
Net loss	—	—	—	—	—	(63,386)	—	(63,386)
<b>Balances at December 31, 2017</b>	—	—	29,658,202	3	263,409	(237,265)	—	26,147
Issuance of common stock upon exercise of stock options	—	—	182,261	—	397	—	—	397
Issuance of common stock in connection with employee stock purchase plan	—	—	81,455	—	297	—	—	297
Issuance of common stock upon public offering, net of issuance costs	—	—	11,596,173	1	61,528	—	—	61,529
Stock-based compensation expense	—	—	—	—	7,483	—	—	7,483
Net loss	—	—	—	—	—	(59,978)	—	(59,978)
<b>Balances at December 31, 2018</b>	—	\$ —	41,518,091	\$ 4	\$ 333,114	\$ (297,243)	\$ —	\$ 35,875

The accompanying notes are an integral part of these consolidated financial statements.

**OCULAR THERAPEUTIX, INC.**  
**CONSOLIDATED STATEMENTS OF CASH FLOWS**  
(In thousands)

	<u>Year Ended December 31,</u>		
	<u>2018</u>	<u>2017</u>	<u>2016</u>
<b>Cash flows from operating activities:</b>			
Net loss	\$ (59,978)	\$ (63,386)	\$ (44,703)
Adjustments to reconcile net loss to net cash used in operating activities			
Stock-based compensation expense	7,483	7,321	5,956
Non-cash interest expense	397	408	371
Depreciation and amortization expense	2,286	1,625	881
(Gain)/loss on disposal of property and equipment	—	(5)	1,269
Purchase of premium on marketable securities	—	(3)	(37)
Amortization of premium on marketable securities	—	17	186
Changes in operating assets and liabilities:			
Accounts receivable	25	24	(57)
Prepaid expenses and other current assets	(260)	45	924
Inventory	(95)	(9)	21
Accounts payable	(796)	932	(159)
Accrued expenses and deferred rent	1,711	2,558	1,389
Deferred revenue	—	—	(42)
Net cash used in operating activities	<u>(49,227)</u>	<u>(50,473)</u>	<u>(34,001)</u>
<b>Cash flows from investing activities:</b>			
Purchases of property and equipment	(1,889)	(8,252)	(1,919)
Proceeds from sale of property and equipment	—	5	2
Purchases of marketable securities	—	(3,000)	(41,699)
Proceeds from maturities of marketable securities	—	38,200	80,684
Net cash (used in) provided by investing activities	<u>(1,889)</u>	<u>26,953</u>	<u>37,068</u>
<b>Cash flows from financing activities:</b>			
Proceeds from issuance of notes payable	12,032	3,700	—
Proceeds from exercise of stock options	397	685	199
Proceeds from issuance of common stock pursuant to employee stock purchase plan	297	276	278
Proceeds from issuance of common stock offering, net	61,571	29,238	627
Payments of insurance costs financed by a third party	—	(591)	(519)
Repayment of notes payable	(5,657)	(1,300)	—
Net cash provided by financing activities	<u>68,640</u>	<u>32,008</u>	<u>585</u>
<b>Net increase in cash, cash equivalents and restricted cash</b>	<b>17,524</b>	<b>8,488</b>	<b>3,652</b>
Cash, cash equivalents and restricted cash at beginning of period	43,152	34,664	31,012
Cash, cash equivalents and restricted cash at end of period	<u>\$ 60,676</u>	<u>\$ 43,152</u>	<u>\$ 34,664</u>
<b>Supplemental disclosure of cash flow information:</b>			
Cash paid for interest	\$ 1,515	\$ 1,461	\$ 1,301
<b>Supplemental disclosure of non-cash investing and financing activities:</b>			
Additions to property and equipment included in accounts payable and accrued expenses at balance sheet dates	\$ 155	\$ 538	\$ 451
Insurance premium financed by a third party	\$ —	\$ —	\$ 722
Public offering costs included in accounts payable and accrued expenses at balance sheet dates	\$ 42	\$ 108	\$ —

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 are 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.

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, uncertainty of market acceptance of products and the need to obtain additional financing. 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, 2018, the Company’s lead product candidate DEXTENZA (dexamethasone insert) 0.4mg, has been approved by the FDA and the 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 rapid change in 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, including to support the planned commercial launch of DEXTENZA.

The Company believes that its existing cash and cash equivalents at December 31, 2018 along with the net proceeds of \$37,100 from the issuance of convertible notes payable issued in March 2019 (Note 19) and the \$4,967 net proceeds obtained from the issuance of common stock in January and February 2019 (Note 19), will enable it to fund its operating expenses, debt service obligations and capital expenditure requirements into early 2020.

Management has determined that the Company’s accumulated deficit, history of losses, negative cash flows from operations and future expected losses raise substantial doubt about the Company’s ability to continue as a going concern within one year of the issuance date of these consolidated financial statements. The Company expects to continue to generate operating losses and negative cash flows from operations in the foreseeable future. As of December 31, 2018, the Company had an accumulated deficit of \$297,243.

While the Company has raised capital in the past, the ability to raise capital in future periods is not considered probable, as defined under the accounting standards and therefore, were not considered in management’s assessment of the Company’s ability to continue as a going concern. The Company expects to seek additional funds through equity or debt financings. If the Company is unable to obtain other financing, the Company would be forced to delay, reduce or eliminate its research and development programs or any future commercialization efforts or to relinquish valuable rights to its technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to the Company. The actions necessary to reduce spending to a level that mitigates the factors

described above are not considered probable, as defined in the accounting standards and therefore were not considered in management's assessment of the Company's ability to continue as a going concern.

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

## **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, the accrual of research and development expenses, including clinical trials, and the valuation of common stock and stock-based awards. 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***

On January 1, 2018, the Company adopted the new revenue standard, Accounting Standards Codification ("ASC") 606 – *Revenue from Contracts with Customers*, which amended revenue recognition principles and provides a single, comprehensive set of criteria for revenue recognition within and across all industries. The Company's adoption of the new revenue standard did not have a material impact on its consolidated financial statements. This new revenue standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. The new revenue standard provides a five-step framework whereby revenue is recognized when control of promised goods or services is transferred to a customer at an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of the new revenue standard, the Company 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) we satisfy a performance obligation. The Company only applies the five-step model to contracts when collectability of the consideration to which the Company is entitled in exchange for the goods or services the Company transfers to the customer is determined to be probable. At contract inception, once the contract is determined to be within the scope of the new revenue standard, the Company assess whether the goods or services promised within each contract are distinct and, therefore, represent a separate performance obligation. Goods and services that are determined not to be distinct are combined with other promised goods and services until a distinct bundle is identified. The Company then allocates the transaction price (the amount of consideration the Company expects to be entitled to from a customer in exchange for the promised goods or services) to each performance obligation and recognizes the associated revenue when (or as) each performance obligation is satisfied.

Amounts are recorded as accounts receivable when the Company's right to consideration is unconditional. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less. The Company expenses incremental costs of obtaining a contract as and when incurred

if the expected amortization period of the asset that the Company would have recognized is one year or less or the amount is immaterial. At December 31, 2018, the Company had not capitalized any costs to obtain any of our contracts.

The Company recognizes revenue on product sales at the time control of the product transfers to the customer. In substantially all of the Company's arrangements, title of its products transfers at shipping point and, as a result, the Company determined control transfers at the point of shipment. In more limited cases, there are destination-based shipping terms and, thus, control is deemed to transfer when the product arrives at the customer site. Incremental costs of obtaining a contract are expensed as and when incurred if the expected amortization period of the asset that would have been recognized is one year or less. Shipping and handling costs are included as a component of cost of product revenue.

Payment terms and conditions vary among the Company's customers, although terms generally include a requirement of payment within 30 days of product shipment. Prior to providing payment terms to customers, an evaluation of the customer's credit risk is performed. Returns and customer credits are infrequent and insignificant and are recorded as a reduction to sales. Rights of return are not included in sales arrangements and, therefore, there is minimal variable consideration included in the transaction price of our products.

### ***Inventory Valuation***

Inventory is valued at the lower of cost or net realizable value, determined by the first-in, first-out ("FIFO") method.

Prior to approval by the Food and Drug Administration ("FDA") or other regulatory agencies of the Company's products, the Company expenses inventory costs in the period incurred as research and development expenses. After such time as the product receives approval, the Company begins to capitalize the inventory costs related to the product. The Company also reviews its inventories for potential obsolescence.

Inventory consisted of the following:

	<b>December 31,</b>	
	<b>2018</b>	<b>2017</b>
Raw materials	\$ 112	\$ 68
Work-in-process	33	37
Finished goods	72	17
	<u>\$ 217</u>	<u>\$ 122</u>

### ***Restricted Cash***

As of December 31, 2018 and 2017, the Company held restricted cash of \$6,614 and \$1,614, respectively, on its consolidated balance sheet. The Company held restricted cash as security deposits for the lease of its manufacturing space and corporate headquarters (Note 13). In 2018, restricted cash increased due to a financial covenant associated with the 2018 Amended Credit Facility which restricts the Company's withdrawal or usage of \$5,000.

### ***Concentration of Credit Risk and of Significant Suppliers***

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and cash equivalents. 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 ReSure Sealant product. The Company's development programs as well as revenue from future sales of ReSure Sealant could be adversely affected by a significant interruption in the supply of any of the components of these products.

### ***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 are carried at fair value determined according to the fair value hierarchy described above (Note 3). The carrying value of accounts receivable, accounts payable and accrued expenses approximate their fair value due to the short-term nature of these assets and liabilities. At December 31, 2018 and 2017, the carrying value of the Company's outstanding notes payable (Note 7) approximates fair value based on the interest rate for the borrowings outstanding.

### ***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. Significant 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.

For stock-based awards granted to consultants and non-employees, compensation expense is recognized over the period during which services are rendered by such consultants and non-employees until completed. At the end of each financial reporting period prior to completion of the service, the fair value of these awards is re-measured using the then-current fair value of the Company's common stock and updated assumption inputs in the Black-Scholes option-pricing model.

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.

### ***Comprehensive Loss***

Comprehensive loss includes net loss as well as other changes in stockholders' equity that result from transactions and economic events other than those with stockholders. For the years ended December 31, 2017 and 2016, other comprehensive loss consisted of unrealized gains (losses) from marketable securities. For the years ended December 31, 2018, there were no items that gave rise to other comprehensive loss and therefore, was no difference between net loss and comprehensive loss.

### ***Net Income (Loss) Per Share***

The Company applies the two-class method which determines net income (loss) per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income available to common stockholders for the period to be allocated between common and participating securities based upon their respective rights to receive dividends as if all income for the period had been distributed.

Basic net income (loss) per share attributable to common stockholders is computed by dividing the net income (loss) attributable to common stockholders by the weighted average number of shares of common stock outstanding for the period. Diluted net income (loss) attributable to common stockholders is computed by adjusting income (loss) attributable to common stockholders to reallocate undistributed earnings based on the potential impact of dilutive securities, including outstanding stock options, unvested restricted common stock, common stock warrants. Diluted net income (loss) per share attributable to common stockholders is computed by dividing the diluted net income (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 outstanding stock options, common stock warrants and unvested restricted common stock.

Restricted stock awards granted by the Company entitle the holder of such awards to dividends declared or paid by the board of directors, regardless of whether such awards are unvested, as if such shares were outstanding common shares at the time of the dividend. However, the unvested restricted stock awards are not entitled to share in the residual net assets (deficit) of the Company. Accordingly, in periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive. The Company reported a net loss attributable to common stockholders for the years ended December 31, 2018, 2017 and 2016.

### ***Deferred Offering Costs***

The Company capitalizes certain legal and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of the equity financing, these costs are recorded as a reduction of the proceeds generated as a result of the offering. Should the planned equity financing be abandoned, the deferred offering costs will be expensed immediately as a charge to operating expense in the consolidated statements of operations and comprehensive loss. There were no deferred offering costs at December 31, 2018. Deferred offering costs amounted to \$108 at December 31, 2017 and are capitalized in prepaid expenses and other current assets.

**Recently Adopted Accounting Pronouncements**

In March 2016, the FASB issued ASU No. 2016-09, Compensation – Stock Compensation (“ASU 2016-09”). ASU 2016-09 identifies areas for simplification involving several aspects of accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, an option to recognize gross stock compensation expense with actual forfeitures recognized as they occur, as well as certain classifications on the statement of cash flows. The amendments in this update became effective for the first interim period within annual reporting periods beginning after December 15, 2016. The Company adopted ASU 2016-09 on January 1, 2017 and continues to estimate forfeitures at each period. The adoption of ASU 2016-09 did not have a material impact to the consolidated financial statements.

The Company adopted the New Revenue Standard on January 1, 2018 using the modified retrospective method. The adoption of the New Revenue Standard did not have a material impact on its consolidated financial statements. Under the New Revenue Standard, the Company recognizes revenue when the customer obtains control of the good in an amount that reflects the consideration which the Company expects to receive in exchange for those goods. The Company only applies the New Revenue Standard to contracts when it is probable that the Company will collect the consideration it is entitled to in exchange for the goods transferred to the customer.

In August 2016, the FASB issued Accounting Standards Update No. 2016-15, Classification of Certain Cash Receipts and Cash Payments (“ASU 2016-15”). ASU 2016-15 is intended to clarify guidance on the classification of certain cash receipts and payments in the statement of cash flows and to eliminate the diversity in practice related to such classifications. The Company adopted ASU 2016-15 effective January 1, 2018 and its adoption did not have a material impact on its consolidated financial statements.

In November 2016, the FASB issued ASU 2016-18, “Statement of Cash Flows (Topic 230) - Restricted Cash” (“ASU 2016-18”). ASU 2016-18 requires a statement of cash flows to explain the change during the period in the total of cash, cash equivalents, and amounts generally described as restricted cash or restricted cash equivalents. Amounts generally described as restricted cash and restricted cash equivalents should be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. The Company adopted ASU 2016-18 effective January 1, 2018 and has reflected the adoption retrospectively to all periods presented. The Company’s statements of cash flows includes 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 consolidated balance sheet that sum to the total of the same amounts shown in the consolidated statement of cash flows:

	December 31, 2018	December 31, 2017	December 31, 2016
Cash and cash equivalents	\$ 54,062	\$ 41,538	\$ 32,936
Restricted cash	6,614	1,614	1,728
Total cash, cash equivalents and restricted cash as shown on the statement of cash flow	<u>\$ 60,676</u>	<u>\$ 43,152</u>	<u>\$ 34,664</u>

In May 2017, the FASB issued ASU 2017-09, “Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting” (“ASU 2017-09”), which clarifies when to account for a change to the terms or conditions of a share-based payment award as a modification. The new standard does not change the accounting for modifications but clarifies that modification accounting guidance should only be applied if the fair value, vesting conditions, or classification of the award changes as a result of the change in terms or conditions. The new standard is effective for fiscal years, and interim periods within, beginning after December 15, 2017. Early adoption is permitted. A reporting entity must apply the amendments in the ASU prospectively to an award modified on or after the adoption date. The Company adopted ASU 2017-09 effective January 1, 2018 and its adoption did not have a material impact on the Company’s consolidated financial statements. The adoption of ASU 2017-09 will have an impact on the accounting for the modification of stock-based awards, if any, to the extent stock-based awards are modified.

### Recently Issued Accounting Pronouncements

In February 2016, the FASB issued ASU No. 2016-02, Leases (ASC 842) (“ASU 2016-02”). ASU 2016-02 requires lessees to recognize most leases on the balance sheet. This is expected to increase both reported assets and liabilities. The new lease standard does not substantially change lessor accounting. The Company adopted the new leasing standard on January 1, 2019, using a modified retrospective transition approach to be applied to leases existing as of, or entered into after, January 1, 2019. The Company elected to apply the package of practical expedients which allows entities not to reassess whether contracts are or contain leases, lease classification, and whether initial direct costs qualify for capitalization. Additionally, the Company elected not to separate lease and non-lease components. The Company’s primary operating leases represent the lease of its corporate headquarters at 15 Crosby and a lease for additional space at 36 Crosby, both in Bedford, Massachusetts. Upon adoption of the new leasing standard, the Company expects to recognize a lease liability of approximately \$9,000 and a related right-of-use asset of approximately \$6,000 on its consolidated balance sheet with the difference being due to the elimination of previously reported lease incentive obligations and deferred rent. The impact of adoption of the new leasing standards will have an immaterial impact to the Company’s consolidated statements of operations and comprehensive loss and cash flows.

### 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, 2018 and 2017 and indicate the level of the fair value hierarchy utilized to determine such fair value:

	Fair Value Measurements as of December 31, 2018 Using:			
	Level 1	Level 2	Level 3	Total
<b>Assets:</b>				
Cash equivalents:				
Money market funds	\$ —	\$ 50,906	\$ —	\$ 50,906
Total	\$ —	\$ 50,906	\$ —	\$ 50,906

	Fair Value Measurements as of December 31, 2017 Using:			
	Level 1	Level 2	Level 3	Total
<b>Assets:</b>				
Cash equivalents:				
Money market funds	\$ —	\$ 40,386	\$ —	\$ 40,386
Total	\$ —	\$ 40,386	\$ —	\$ 40,386

During the years ended December 31, 2018, 2017 and 2016, there were no transfers between Level 1, Level 2 and Level 3.

#### 4. Property and Equipment, net

Property and equipment, net consisted of the following:

	December 31,	
	2018	2017
Equipment	\$ 7,917	\$ 6,183
Leasehold improvements	8,675	8,553
Furniture and fixtures	760	740
Software	180	118
Construction in progress	331	225
	17,863	15,819
Less: Accumulated depreciation	(7,627)	(5,341)
	<u>\$ 10,236</u>	<u>\$ 10,478</u>

Depreciation expense was \$2,286, \$1,625 and \$881 for the years ended December 31, 2018, 2017 and 2016, respectively.

For the year ended December 31, 2016, the Company wrote off \$1,263 of manufacturing equipment that was included in construction in progress at December 31, 2015.

#### 5. Accrued Expenses and Deferred Rent

Accrued expenses consisted of the following:

	December 31, 2018	December 31, 2017
Accrued payroll and related expenses	\$ 3,558	\$ 2,936
Accrued rent	267	267
Accrued professional fees	1,393	534
Accrued research and development expenses	380	217
Accrued other	596	356
	<u>\$ 6,194</u>	<u>\$ 4,310</u>

#### 6. Collaboration and Feasibility Agreements

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 products that deliver small molecule drugs, including TKIs for any target including VEGF, or any product that deliver 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 under its intellectual property 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, which it initiated in early 2018.

If Regeneron decided to exercise the Option, Regeneron will 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. In December 2017, the Company delivered to Regeneron the final formulation for Regeneron's initial preclinical tolerability study. Although the Company is engaged in ongoing discussions with Regeneron, Regeneron has not informed the Company of its decision to exercise the Option. Pending a decision from Regeneron, the Company is not actively pursuing further formulation development or other preclinical testing under the Collaboration Agreement. 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.

## **7. Notes Payable**

The Company entered into a credit and security agreement in 2014 (the "2014 Credit Facility") which most recently was amended in March 2017 and in December 2018 has a total borrowing capacity of \$25,000 which has been fully drawn down.

In March 2017, the Company amended (the "2017 Amended Credit Facility") the terms of its debt with existing lenders for total indebtedness of \$18,000, which was used primarily to pay-off outstanding balances as of the closing date. The interest only period was extended through February 1, 2018. The Company was obligated to make interest-only payments under the 2017 Amended Credit Facility until February 1, 2018. Thereafter, it was required to make monthly principal and interest payments through December 1, 2020. Amounts borrowed under the Amended Credit Facility were at LIBOR base rate, subject to 1.00% floor, plus 7.25% with an indicative interest rate of 8.25% as of the amendment date. In addition, a final payment equal to 3.5% of amounts drawn under the Amended Credit Facility was due upon the maturity date of December 1, 2020.

In December 2018, the Company amended (the "2018 Amended Credit Facility") the terms of its debt with existing lenders for total indebtedness of \$25,000, which was used primarily to pay-off outstanding balances as of the closing date. The Company is required to make interest-only payments under the 2018 Amended 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. In the event the Company achieves certain milestones under the 2018 Amended Credit Facility, the Company has the right to extend the interest-only payments through December 21, 2021 and make 24 equal monthly installments of principal in the amount of \$1,042, plus interest. The Company has not assumed the achievement of these milestones for purposes of disclosures herein.

Amounts borrowed under the 2018 Amended Credit Facility 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%. In addition, a final payment (exit fee) equal to 3.5% of amounts drawn under the Amended 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.

The Company accounted for the 2017 and 2018 Amended Credit Facility as a modification in accordance with the guidance in ASC 470-50, Debt. Amounts paid to the lenders were recorded as debt discount and a new effective interest rate was established. The effective annual interest rate of the outstanding debt under the Amended Credit Facility is 13.9%.

Under the 2018 Amended Credit Facility the Company is required to maintain a minimum of \$5,000 of cash on hand as a financial covenant to the borrowing arrangement, which the Company has included in long-term restricted cash in the accompanying consolidated balance sheet. There are no other financial covenants associated with the 2018 Amended Credit Facility; 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. The Company is not in violation of any of the covenants. The obligations under the 2018 Amended Credit Facility 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.

Borrowings outstanding are as follows:

	<u>December 31, 2018</u>	<u>December 31, 2017</u>
Borrowings outstanding	\$ 25,000	\$ 18,000
Accrued exit fee	5	221
Unamortized discount	(217)	(205)
	<u>\$ 24,788</u>	<u>\$ 18,016</u>

As of December 31, 2018, the annual repayment requirements for the 2018 Amended Credit Facility, inclusive of interest and the final payment of \$875 due at expiration, were as follows:

<u>Year Ending December 31,</u>	<u>Principal</u>	<u>Interest and Final Payment</u>	<u>Total</u>
2019	\$ —	\$ 2,474	\$ 2,474
2020	—	2,481	2,481
2021	8,333	2,094	10,427
2022	8,333	1,270	9,603
2023	8,334	1,319	9,653
	<u>\$ 25,000</u>	<u>\$ 9,638</u>	<u>\$ 34,638</u>

## 8. Warrants

The Company has warrants for the purchase of 18,939 shares of common stock outstanding at December 31, 2018 at a weighted average exercise price of \$7.92 per share and an expiration date of April 17, 2021.

## 9. 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, 2018.

## 10. Common Stock

The Amended and Restated Certificate of Incorporation authorized 100,000,000 shares of the Company's common stock. Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders.

In 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 fourth quarter of 2016, the Company sold 102,077 shares of common stock under the 2016 Sales Agreement resulting in net proceeds of approximately \$626 after underwriting discounts, commission and other offering expenses. During the year ended December 31, 2017, the Company sold 788,491 shares of common stock under the 2016 Sales Agreement, resulting in net proceeds of approximately \$5,977 after underwriting discounts and commissions. 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 has sold 5,011,741 shares of common stock at-the-market under the 2016 Sales Agreement, resulting in net proceeds of approximately \$33,427 after underwriting discounts, commissions and expenses.

In January 2017, the Company completed a follow-on offering of its common stock at a public offering price of \$7.00 per share. The offering consisted of 3,571,429 shares of common stock sold by the Company. The Company received net proceeds from the follow-on offering of \$23,261 after deducting underwriting discounts, commissions and expenses.

In January 2018, the Company completed a follow-on offering of its common stock at a public offering price of \$5.00 per share. The offering consisted of 7,475,000 shares of common stock sold by the Company, including those shares sold in connection with the exercise by the underwriter of its option to purchase additional shares. The Company received net proceeds from the follow-on offering of \$34,704 after deducting underwriting discounts, commissions and expenses.

As of December 31, 2018, the Company had reserved 7,232,523 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"), the number of shares available for issuance under the 2014 Employee Stock Purchase Plan (Note 11), and the outstanding warrants to purchase common stock (Note 8).

## **11. 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, 2018, the number of shares available for issuance under the 2014 Plan increased by 1,186,328. As of December 31, 2018, 1,581,243 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. Prior to the IPO, the value of common stock was determined by the board of directors by taking into consideration its most recently available valuation of common shares performed by management and the board of directors as well as additional factors which might have changed since the date of the most recent contemporaneous valuation through 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 Stock Incentive Plan as an inducement material to Mr. Mattessich's acceptance of entering into employment with the Company in accordance with Nasdaq Listing Rule 5635(c)(4).

### ***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, 2018, the number of shares available for issuance under the 2014 Plan increased by 148,291. As of December 31, 2018, 401,510 shares of common stock remain 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 Company estimates its expected stock volatility based on the historical volatility of a publicly traded set of peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. Beginning in 2016, the Company estimates its expected volatility using a weighted average of the historical volatility of its publicly traded peer companies and the volatility of its common stock, and expect to continue to do so until such time as the Company has adequate historical data regarding the volatility of its traded stock price. The expected term of the Company's stock options to employees has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. 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, 2018, there were outstanding unvested service-based stock options held by nonemployees for the purchase of 7,917 shares of common stock.

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,		
	2018	2017	2016
Risk-free interest rate	2.65 %	2.00 %	1.42 %
Expected term (in years)	6	6	6
Expected volatility	102 %	102 %	85 %
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
<b>Outstanding as of December 31, 2017</b>	4,002,374	\$ 10.08	7.2	\$ 1,222
Granted	1,883,157	5.59		
Exercised	(182,261)	2.18		
Forfeited	(472,439)	10.83		
<b>Outstanding as of December 31, 2018</b>	<u>5,230,831</u>	\$ 8.67	7.5	\$ 654
<b>Options vested and expected to vest as of December 31, 2018</b>	<u>4,954,183</u>	\$ 8.82	7.4	\$ 654
<b>Options exercisable as of December 31, 2018</b>	<u>2,629,571</u>	\$ 10.57	6.2	\$ 654

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 \$551, \$408 and \$575 during the years ended December 31, 2018, 2017 and 2016, respectively.

The weighted average grant date fair value of stock options granted to employees and directors during the years ended December 31, 2018, 2017, 2016 was \$4.48, \$6.44 and \$4.52 per share, respectively.

### **Restricted Common Stock**

The 2006 and 2014 Plans provide for the award of restricted common stock. The Company has granted restricted common stock with time-based vesting conditions. Unvested shares of restricted common stock may not be sold or transferred by the holder. These restrictions lapse according to the time-based vesting conditions of each award.

The aggregate intrinsic value of restricted stock awards is calculated as the positive difference between the prices paid, if any, of the restricted stock awards and the fair value of the Company's common stock. There was no aggregate intrinsic value of restricted stock awards that vested during the years ended December 31, 2018, 2017 and 2016 and there was no remaining restricted shares at December 31, 2018 and 2017.

### **Stock-based Compensation**

The Company recorded stock-based compensation expense related to stock options, vesting of restricted common stock and grants of common stock in the following expense categories of its statements of operations:

	<u>Year Ended December 31,</u>		
	<u>2018</u>	<u>2017</u>	<u>2016</u>
Research and development	\$ 2,557	\$ 2,584	\$ 1,900
Selling and marketing	449	633	490
General and administrative	4,477	4,104	3,566
	<u>\$ 7,483</u>	<u>\$ 7,321</u>	<u>\$ 5,956</u>

As of December 31, 2018, the Company had an aggregate of \$11,486 of unrecognized stock-based compensation cost, which is expected to be recognized over a weighted average period of 2.5 years.

## **12. 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, 2018, 2017 and 2016:

	<u>Year Ended December 31,</u>		
	<u>2018</u>	<u>2017</u>	<u>2016</u>
<b>Numerator:</b>			
Net loss attributable to common stockholders	\$ (59,978)	\$ (63,386)	\$ (44,703)
<b>Denominator:</b>			
Weighted average common shares outstanding, basic and diluted	38,115,142	28,818,196	24,816,348
Net loss per share attributable to common stockholders, basic and diluted	<u>\$ (1.57)</u>	<u>\$ (2.20)</u>	<u>\$ (1.80)</u>

The Company excluded the following common stock equivalents, outstanding as of December 31, 2018, 2017, and 2016, from the computation of diluted net loss per share attributable to common stockholders for the years ended December 31, 2018, 2017 and 2016 because they had an anti-dilutive impact due to the net loss incurred for the periods.

	<u>December 31,</u>		
	<u>2018</u>	<u>2017</u>	<u>2016</u>
Options to purchase common stock	5,230,831	4,002,374	3,091,480
Warrants for the purchase of common stock	18,939	18,939	18,939
	<u>5,249,770</u>	<u>4,021,313</u>	<u>3,110,419</u>

## **13. Commitments and Contingencies**

### **Leases**

The Company leases office, laboratory and manufacturing space in Bedford, Massachusetts and certain office equipment under non-cancelable operating leases that expire in July 2023 and July 2027.

Future minimum lease payments for its operating leases as of December 31, 2018 are as follows:

<u>Year Ending December 31,</u>	
2019	1,809
2020	1,850
2021	1,886
2022	1,936
2023	1,730
Thereafter	5,224
Total	<u>\$ 14,435</u>

In October 2017, the Company and CCC Investors LLC (the “Landlord”) entered into an amendment (the “Second 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 Second Amendment amends the original lease agreement and extends the term of the Lease for 36 Crosby Drive from June 30, 2018 to July 31, 2023. Further, the Second Amendment acknowledges that the Company has previously vacated and surrendered, and the Lease has expired with regards to, 34 Crosby Drive, which reduces the Company’s required security deposit under the Lease from \$228 to \$114. Under the Second Amendment, the annual base rent for 36 Crosby Drive shall be approximately \$524 until June 30, 2018, was \$0 from July 1, 2018 to July 31, 2018, and shall be approximately \$544 from August 1, 2018 to July 31, 2019. The annual base rent shall increase annually thereafter. The Second Amendment also provides the Company a one-time option to terminate the Lease on July 31, 2021, upon the Company’s delivery to the Landlord on or before July 31, 2020 of a termination notice and the payment to the Landlord of a termination fee of approximately \$273.

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 in Bedford, Massachusetts. The lease term commenced on February 1, 2017 and will expire on July 31, 2027. The Company relocated its corporate headquarters to the new leased premises during June 2017 and is evaluating the potential relocation of its manufacturing operations to the new leased premises. No base rent was due under the lease until August 1, 2017. The initial annual base rent is approximately \$1,200 and will increase annually beginning on February 1 of each year. The Company is obligated to pay all real estate taxes and costs related to the premises, including costs of operations, maintenance, repair, and replacement and management of the new leased premises. The Company posted a customary letter of credit in the amount of approximately \$1,500 as a security deposit. The lease agreement allows for a landlord provided construction allowance not to exceed approximately \$2,800 to be applied to the total construction costs of the new leased premises. The construction allowance was to be used on or before December 31, 2017, or it would be deemed forfeited with no further obligation by the landlord of the new leased premises. As of December 31, 2017, the Company has billed the landlord for \$2,725 and received payments of \$2,656 from the landlord. The Company forfeited \$0.1 million under the construction allowance. Build out costs being reimbursed under the tenant improvement allowance have been recorded as deferred rent and will be amortized as a deduction to rent expense over the lease term.

The Company recognizes rent expense on a straight-line basis over the lease period and has recorded deferred rent for rent expense incurred but not yet paid. During the years ended December 31, 2018, 2017 and 2016, the Company recognized \$1,788, \$1,733 and \$1,084, respectively, of rental expense, related to its office, laboratory and manufacturing space and office equipment.

#### ***Intellectual Property Licenses***

The Company has a license agreement with Incept, LLC (“Incept”) (Note 16) 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, 2018, royalties paid under this agreement related to product sales were \$214.

On September 13, 2018, (the “Effective Date”) 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. The Company does not believe that the outcome of any claims under indemnification arrangements will 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, 2018.

### ***Purchase Commitments***

Purchase commitments represent non-cancelable contractual commitments associated with certain clinical trial activities within the Company’s clinical research organization.

### ***Manufacturing Commitments***

Manufacturing contracts generally provide for termination on notice, and therefore are cancelable contracts but are contracts that the Company is likely to continue, regardless of the fact that they are cancelable.

### ***Collaboration Agreement***

On October 10, 2016, the Company entered into a Collaboration Agreement with Regeneron (Note 6). If the Option to enter into an exclusive worldwide license is exercised, Regeneron will 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. Through December 31, 2018, the Option has not been exercised and no payments have been made to Regeneron.

### ***Legal Proceedings***

#### ***Securities Class Actions***

On July 7, 2017, a putative class action lawsuit was filed against the Company and certain of the Company’s current and former executive officers in the United States District Court for the District of New Jersey, captioned *Thomas Gallagher v. Ocular Therapeutix, Inc, et al.*, Case No. 2:17-cv-05011. The complaint purports to be brought on behalf of shareholders who purchased the Company’s common stock between May 5, 2017 and July 6, 2017. The

complaint generally alleges that the Company and certain of the Company's current and former officers violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934 ("Exchange Act") and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning the Form 483 issued by the FDA related to DEXTENZA and the Company's manufacturing operations for DEXTENZA. The complaint seeks unspecified damages, attorneys' fees, and other costs. On July 14, 2017, an amended complaint was filed; the amended complaint purports to be brought on behalf of shareholders who purchased the Company's common stock between May 5, 2017 and July 11, 2017, and otherwise includes allegations similar to those made in the original complaint.

On July 12, 2017, a second putative class action lawsuit was filed against the Company and certain of the Company's current and former executive officers in the United States District Court for the District of New Jersey, captioned *Dylan Caraker v. Ocular Therapeutix, Inc., et al.*, Case No. 2:17-cv-05095. The complaint purports to be brought on behalf of shareholders who purchased the Company's common stock between May 5, 2017 and July 6, 2017. The complaint includes allegations similar to those made in the *Gallagher* complaint, and seeks similar relief.

On August 3, 2017, a third putative class action lawsuit was filed against the Company and certain of the Company's current and former executive officers in the United States District Court for the District of New Jersey, captioned *Shawna Kim v. Ocular Therapeutix, Inc., et al.*, Case No. 2:17-cv-05704. The complaint purports to be brought on behalf of shareholders who purchased the Company's common stock between March 10, 2016 and July 11, 2017. The complaint includes allegations similar to those made in the *Gallagher* complaint, and seeks similar relief.

On October 27, 2017, a magistrate judge for the United States District Court for the District of New Jersey granted the defendants' motion to transfer the above-referenced *Gallagher*, *Caraker*, and *Kim* litigations to the United States District Court for the District of Massachusetts. These matters were assigned the following docket numbers in the District of Massachusetts: 1:17-cv-12288 (*Gallagher*), 1:17-cv-12146 (*Caraker*), and 1:17-cv-12286 (*Kim*).

On March 9, 2018, the court consolidated the three actions and appointed co-lead plaintiffs and co-lead counsel for the consolidated action. On May 7, 2018, co-lead plaintiffs filed a consolidated amended class action complaint. The amended complaint makes allegations similar to those in the original complaints, against the same defendants, and seeks similar relief on behalf of shareholders who purchased the Company's common stock between March 10, 2016 and July 11, 2017. The amended complaint generally alleges that defendants violated Sections 10(b) and/or 20(a) of the Exchange Act and Rule 10b-5 promulgated thereunder. On July 6, 2018, defendants filed a motion to dismiss the consolidated amended complaint. Plaintiffs' filed an opposition to the motion to dismiss on September 4, 2018, and defendants filed a reply on October 4, 2018. The court held oral argument on the motion to dismiss on February 6, 2019 and took the matter under advisement.

The Company denies any allegations of wrongdoing and intends to vigorously defend against these lawsuits.

#### *Shareholder Derivative Litigation*

On July 11, 2017, a purported shareholder derivative lawsuit was filed against certain of the Company's current and former executive officers, certain current and former board members, and the Company as a nominal defendant, in the United States District Court for the District of Massachusetts, captioned *Robert Corwin v. Sawhney et al.*, Case No. 1:17-cv-11270. The complaint generally alleged that the individual defendants breached fiduciary duties owed to the Company by making allegedly false and/or misleading statements concerning the Form 483 related to DEXTENZA and our manufacturing operations for DEXTENZA. The complaint purported to assert claims against the individual defendants for breach of fiduciary duty, and sought to recover on behalf of the Company for any liability the Company incurs as a result of the individual defendants' alleged misconduct. The complaint also sought contribution on behalf of the Company from all individual defendants for their alleged violations of Sections 10(b) and/or 20(a) of the Exchange Act and Rule 10b-5 promulgated thereunder. The complaint sought declaratory, equitable, and monetary relief, an unspecified amount of damages, with interest, and attorneys' fees and costs. On September 20, 2017, counsel for the plaintiff filed a notice of voluntary dismissal, stating that the plaintiff wished to coordinate his efforts and proceed in a consolidated fashion with the plaintiff in a similar derivative suit that was pending in the Superior Court of Suffolk County of the Commonwealth of Massachusetts captioned *Angel Madera v. Sawhney et al.*, Case No. 17-2273 (which is discussed in the paragraph immediately below) by filing an action in that court subsequent to the dismissal of this lawsuit. The Corwin lawsuit was dismissed without prejudice on September 21, 2017. On October 24, 2017, the plaintiff filed a new derivative complaint in Massachusetts Superior Court (Suffolk County), captioned *Robert Corwin v. Sawhney et al.*, Case No. 17-3425 (BLS2). The new *Corwin* complaint includes allegations similar to those made in the

federal court complaint and asserts a derivative claim for breach of fiduciary duty against certain of our current and former officers and directors. The complaint also asserts an unjust enrichment claim against two additional defendants, SV Life Sciences Fund IV, LP and SV Life Sciences Fund IV Strategic Partners, LP. The complaint also names the Company as a nominal defendant.

On July 19, 2017, a second purported shareholder derivative lawsuit was filed against certain of the Company's current and former executive officers, all current board members, one former board member, and the Company as a nominal defendant, in the Superior Court of Suffolk County of the Commonwealth of Massachusetts, captioned *Angel Madera v. Sawhney et al.*, Case. No. 17-2273. The complaint included allegations similar to those made in the *Corwin* complaint. The complaint purported to assert derivative claims against the individual defendants for breach of fiduciary duty, unjust enrichment, abuse of control, gross mismanagement, and waste of corporate assets, and sought to recover on behalf of the Company for any liability the Company incurs as a result of the individual defendants' alleged misconduct. The complaint sought declaratory, equitable, and monetary relief, an unspecified amount of damages, with interest, and attorneys' fees and costs. On November 6, 2017, the court dismissed this action without prejudice due to plaintiff's failure to complete service of process within the time permitted under applicable court rules. On December 21, 2017, the same plaintiff filed a new derivative complaint in the same court, captioned *Angel Madera v. Sawhney et al.*, Case. No. 17-4126 (BLS2). The new *Madera* complaint is premised on substantially similar allegations as the previous complaint and purports to assert derivative claims against certain current and former executive officers and board members for breach of fiduciary duty, unjust enrichment, and waste of corporate assets, and names the Company as a nominal defendant. Like the new *Corwin* complaint, the new *Madera* complaint also asserts an unjust enrichment claim against two additional defendants, SV Life Sciences Fund IV, LP and SV Life Sciences Fund IV Strategic Partners, LP.

By order dated January 29, 2018, the court consolidated the state court *Corwin* and *Madera* complaints under the *Corwin* docket and appointed lead counsel for plaintiffs. On February 28, 2018, plaintiffs filed a consolidated amended complaint. The consolidated complaint names substantially the same defendants and is premised on substantially similar allegations as the previous *Corwin* and *Madera* complaints, asserting claims for breach of fiduciary duty against the individual defendants and unjust enrichment against the two SV entity defendants. On April 17, 2018, all defendants served a motion to dismiss the consolidated amended complaint. On June 22, 2018, plaintiffs served their opposition to the motion to dismiss and a cross-motion to stay the proceedings pending a decision on the motion to dismiss in the above-referenced securities class action in the District of Massachusetts. On July 30, 2018, the parties filed a joint motion to stay the proceedings pending a decision on the motion to dismiss in the above-referenced securities class action in the District of Massachusetts. On August 3, 2018, the court granted the motion to stay.

On January 31, 2018, a third purported shareholder derivative suit was filed against certain of the Company's current and former executive officers, certain current and former board members, and the Company as a nominal defendant, in the United States District Court for the District of Massachusetts, captioned *Brian Robinson v. Sawhney et al.*, Case. No. 1:18-cv-10199. The complaint includes allegations similar to those made in the *Corwin* and *Madera* complaints. The complaint does not name either SV Life Sciences Fund, IV, LP or SV Life Sciences Fund IV Strategic Partners, LP as defendants, and adds two former officers as defendants. The complaint purports to assert derivative claims against the individual defendants for breach of fiduciary duty, waste of corporate assets, and unjust enrichment, and seeks to recover on behalf of the Company for any liability the Company incurs as a result of the individual defendants' alleged misconduct. The complaint seeks declaratory, equitable, and monetary relief, an unspecified amount of damages, with interest, and attorneys' fees and costs. On April 30, 2018, all defendants filed a motion to dismiss or stay the complaint. Plaintiff filed his opposition on June 22, 2018. On July 26, 2018, the parties filed a joint motion to extend the deadline for defendants to file their reply brief pending the potential substitution of the named shareholder plaintiff. On August 20, 2018, the parties filed a joint stipulation and proposed order regarding plaintiff's unopposed request to substitute a new shareholder plaintiff and the parties' joint request that the court stay the proceedings pending a decision on the motion to dismiss in the above-referenced securities class action in the District of Massachusetts. On September 4, 2018, the court entered the requested order substituting the named plaintiff and staying the matter.

On February 16, 2018, a fourth purported shareholder derivative suit was filed against certain of the Company's current and former executive officers, certain current and former board members, and the Company as a nominal defendant, in the United States District Court for the District of Delaware, captioned *Terry Kelly v. Sawhney et al.*, Case. No. 1:18-cv-00277. The complaint includes allegations similar to those made in the *Corwin* and *Madera* complaints. The complaint purports to assert derivative claims against the individual defendants for breach of fiduciary duty, unjust enrichment and waste of corporate assets, and seeks to recover on behalf of the Company for any liability the Company incurs as a result of the individual defendants' alleged misconduct. The complaint also asserts an unjust enrichment

claim against SV Life Sciences Fund IV, LP and SV Life Sciences Fund IV Strategic Partners, LP. The complaint seeks declaratory, equitable, and monetary relief, an unspecified amount of damages, with interest, and attorneys' fees and costs. On June 11, 2018, the parties filed a stipulation staying the lawsuit pending final judgment in the consolidated derivative action pending in Massachusetts state court under the *Corwin* docket, described above. The court entered an order staying the case on June 12, 2018.

The Company denies any allegations of wrongdoing and intend to vigorously defend against these lawsuits.

In addition, the Company has received a subpoena from the SEC, dated December 15, 2017, requesting documents and information concerning DEXTENZA (dexamethasone insert) 0.4mg, including related communications with the FDA, investors and others. The Company received a second subpoena from the SEC on August 21, 2018, requesting documents and information concerning its participation in two investor conferences in June 2017. The Company intends to fully cooperate with the SEC regarding this non-public, fact-finding inquiry. The SEC has informed the Company that this inquiry should not be construed as an indication that any violations of law have occurred or that the SEC has any negative opinion of any person, entity or security.

The Company is unable to predict the outcome of these lawsuits or proceedings at this time. Moreover, any conclusion of these matters in a manner adverse to the Company and for which it incurs substantial costs or damages not covered by our directors' and officers' liability insurance would have a material adverse effect on the Company's financial condition and business. In addition, the proceedings could adversely impact the Company's reputation and divert management's attention and resources from other priorities, including the execution of business plans and strategies that are important to the Company's ability to grow the Company's business, any of which could have a material adverse effect on the Company's business.

#### **14. Income Taxes**

##### *2017 U.S. Tax Reform*

On December 22, 2017 President Trump signed into law the "Tax Cuts and Jobs Act" ("TCJA") that significantly reforms the Internal Revenue Code of 1986, as amended. The TCJA, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21% effective as of January 1, 2018. Additionally, the TCJA contained provisions for the limitation of the tax deduction for interest expense; limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks in each case for losses arising in taxable years beginning after December 31, 2017(though any such tax losses may be carried forward indefinitely); and modifying or repealing many business deductions and credits. This includes reducing the business tax credit for certain clinical testing expenses incurred in the testing of certain drugs for rare disease or conditions generally referred to as 'orphan drugs'.

The staff of the Securities and Exchange Commission issued Staff Accounting Bulletin No. 118 to address the application of U.S. GAAP in situations when a registrant does not have the necessary information available, prepared or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of the TCJA. In connection with the initial analysis of the impact of the TCJA, the Company remeasured its deferred tax assets and liabilities based on the rates at which they are expected to reverse in the future, which is generally 21%. The remeasurement of the Company's deferred tax assets and liabilities was offset by a corresponding change in the valuation allowance for the year ended December 31, 2017. As a result, there was no impact to the Company's consolidated statements of operations and comprehensive loss as a result of the reduction in tax rates. The other provisions of the TCJA did not have a material impact on the Company's consolidated financial statements. The Company's final determination of the TCJA impact and the remeasurement of its deferred assets and liabilities was completed prior to the deadline of one year from the enactment of the TCJA. For the year ended December 31, 2018, there were no material changes to the analysis originally performed as of December 31, 2017.

### Income Taxes

During the years ended December 31, 2018, 2017 and 2016, 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:

	<b>Year Ended December 31,</b>		
	<b>2018</b>	<b>2017</b>	<b>2016</b>
Federal statutory income tax rate	(21.0)%	(34.0)%	(34.0)%
Tax reform change	—	43.0	—
Research and development tax credits	(3.6)	(3.3)	(2.9)
State taxes, net of federal benefit	(4.5)	(3.8)	(4.8)
Stock-based compensation	1.3	2.2	1.4
Other	0.1	(0.2)	(0.6)
Change in deferred tax asset valuation allowance	27.7	(3.9)	40.9
Effective income tax rate	<u>— %</u>	<u>— %</u>	<u>— %</u>

Net deferred tax assets consisted of the following:

	<b>December 31,</b>	
	<b>2018</b>	<b>2017</b>
Net operating loss carryforwards	\$ 49,699	\$ 33,094
Tax credit carryforwards	10,160	7,971
Capitalized start-up costs	870	1,022
Capitalized research and development expenses, net	18,418	21,869
Accrued expenses and other temporary differences	5,196	3,770
Total gross deferred tax assets	<u>84,343</u>	<u>67,726</u>
Valuation allowance	<u>(84,343)</u>	<u>(67,726)</u>
Net deferred tax assets	<u>\$ —</u>	<u>\$ —</u>

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2018, 2017 and 2016 related primarily to the increase in net operating loss carryforwards, capitalized research and development expenses and research and development tax credit carryforwards offset in 2017 by a decrease in a deferred tax asset resulting from the decreased federal corporate tax rate and were as follows:

	<b>Year Ended December 31,</b>		
	<b>2018</b>	<b>2017</b>	<b>2016</b>
Valuation allowance as of beginning of year	\$ 67,726	\$ 70,236	\$ 51,969
Increases recorded to income tax provision	16,617	24,773	18,267
Decreases recorded to income tax provision	—	(27,283)	—
Valuation allowance as of end of year	<u>\$ 84,343</u>	<u>\$ 67,726</u>	<u>\$ 70,236</u>

As of December 31, 2018, the Company had net operating loss carryforwards for federal and state income tax purposes of \$190,555 and \$161,837, respectively. The federal and state net operating losses generated for annual periods prior to January 1, 2018 begin to expire in 2026. The Company's federal net operating losses generated for the year ended December 31, 2018, which amounted to \$64,327, can be carried forward indefinitely. As of December 31, 2018, the Company also had available research and development tax credit carryforwards for federal and state income tax purposes of \$7,036 and \$3,611, respectively, which begin to expire in 2026 and 2025, respectively. Utilization of the net operating loss 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 net operating loss 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 net operating loss 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, 2018 and 2017. The valuation allowance increased by approximately \$16,617 in 2018 as a result of the increase in deferred tax assets primarily related to net operating loss carryforwards. In 2017, the valuation allowance, on a net basis, decreased by approximately \$2,510 due to the decrease in corporate tax rate offset by an increase in deferred tax assets related to net operating loss carryforwards.

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2018 or 2017.

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, 2015 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, 2018 and 2017, 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.

#### **15. 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, 2018, no contributions have been made to the plan by the Company.

#### **16. Related Party Transactions**

The Company has a license agreement with Incept to use and develop certain patent rights that it entered into in 2007. Royalties incurred and payable to Incept have not been material to date. The Company's former President and Chief Executive Officer and current Executive Chairman and Chairman of the Company's board of directors is a general partner of Incept.

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. The Company's Senior Vice President, Technical Operations, Kevin Hanley, who joined the Company in January 2018, is married to a partner at McCarter, who has not participated in providing legal services to the Company. The Company incurred fees for legal services rendered by McCarter of \$1,019 and \$42 for the year ended December 31, 2018 and 2017, respectively. As of December 31, 2018, there was \$526 recorded in accounts payable for McCarter.

In March 2016, the Company entered into a Master Services Agreement with Axtria, Inc. ("Axtria"). In March 2016, the Company entered into a statement of work totaling approximately \$104 under which Axtria would provide certain sales and marketing analytics to the Company. In February 2017, the Company entered into a separate statement of work totaling approximately \$1,400 under which Axtria would provide data warehouse implementation, operations and maintenance support services to the Company. Jaswinder Chadha, co-founder and CEO of Axtria, is also a member of the Company's Board of Directors and a cousin to the Company's Executive Chairman of the Board of Directors and former President and Chief Executive Officer. For the years ended December 31, 2017 and 2016, payments paid to

Axtria were \$864 under the 2017 statement of work and \$150 under the 2016 statement of work, respectively. As of December 31, 2017, there were no amounts due in accounts payable to Axtria. On July 20, 2017, the Company terminated the 2017 and 2016 statements of work with Axtria.

Since 2014, the Company has engaged Wilmer Cutler Pickering Hale and Dorr LLP (“WilmerHale”) to provide legal services to the Company, including with respect to general corporate, finance, securities law, regulatory and licensing matters. The Company’s former Chief Medical Officer, Jonathan H. Talamo, M.D., who served as Chief Medical Officer from July 2016 until his resignation in June 2017, is married to a partner at WilmerHale, who has not participated in providing legal services to the Company. The Company incurred fees for legal services rendered by WilmerHale of \$1,368 and \$874 for the year ended December 31, 2017 and 2016, respectively. As of December 31, 2017, there was \$194, recorded in accounts payable for WilmerHale. As of December 31, 2017, there was \$80, recorded in accrued expenses for WilmerHale.

## **17. Restructuring and Other Costs**

On July 31, 2017, the Board of Directors approved a strategic restructuring to eliminate a portion of the Company’s workforce as part of an initiative to enhance operations and reduce expenses. As part of this strategic restructuring, the Company eliminated 30 positions across the organization. During the twelve months ended December 31, 2017, the Company recorded \$1,703 of restructuring-related costs in operating expenses in research and development and selling and marketing, including employee severance, benefits and related costs.

On July 31, 2017, the Company entered into a transition, separation and release of claims agreement (the “Ankerud Transition Agreement”), pursuant to which Eric Ankerud resigned from his role as Executive Vice President, Regulatory, Quality and Compliance of the Company, effective immediately. Mr. Ankerud continued to serve as an at-will employee of the Company in the capacity of Senior Advisor until October 31, 2017. He currently serves as a consultant to the Company. Under the Ankerud Transition Agreement, Mr. Ankerud is entitled to separation benefits until October 31, 2018, in the form of continuation of his base salary in the same amount in effect as of October 31, 2018; the payment of monthly premiums for healthcare and/or dental coverage; and provided he continues to provide services to the Company as a consultant, the continued vesting of his outstanding stock options awards in accordance with the applicable equity plans and stock option agreements. During the twelve months ended December 31, 2017, the Company recorded \$386 of severance expense which are included in operating expenses in research and development.

On October 13, 2017, the Company entered into a transition, separation and release of claims agreement (the “Fortune Transition Agreement”) with James Fortune, pursuant to which Mr. Fortune resigned from his role as Chief Operating Officer and any and all other positions he holds as an officer or employee of the Company, effective December 31, 2017 (the “Separation Date”). Pursuant to the Fortune Transition Agreement, effective as of October 13, 2017, the Employment Agreement, by and between the Company and Mr. Fortune, dated June 19, 2014, was terminated. Under the Fortune Transition Agreement, Mr. Fortune will be entitled to separation benefits in the form of (i) the continuation of his base salary for twelve months after the Separation Date in the same amount in effect as of the October 13, 2017 and (ii) the payment of monthly premiums for healthcare and/or dental coverage at the same rate that is in effect on the Separation Date until the earlier of twelve months from the Separation Date or the date Mr. Fortune becomes eligible to receive such benefits under another employer’s benefit plan. Should any annual bonus payments be made to active Company executives for the calendar year 2017, Mr. Fortune will also be eligible to receive a bonus payment in such amount, if any, he would have received had he remained employed with the Company through the date of such bonus payments. During the twelve months ended December 31, 2017, the Company recorded \$417 of severance expense which are included in operating expenses in general and administration.

The following table summarizes the restructuring and other costs by category during the twelve months ended December 31, 2017:

	<b>Twelve Months Ended December 31, 2017</b>	
	<b>Total</b>	
Research and development	\$	690
Selling and marketing		1,399
General and administration		417
	<b>\$</b>	<b>2,506</b>

The following table summarizes the restructuring and other costs reserve for the periods indicated:

	<b>Year Ended December 31, 2018</b>	
Restructuring and other costs at December 31, 2017	\$	960
Amounts paid during the period		(960)
Restructuring and other costs at December 31, 2018	<b>\$</b>	<b>—</b>

### 18. Selected Quarterly Financial Data (Unaudited)

	<b>Three Months Ended</b>							
	<b>Dec. 31, 2018</b>	<b>Sept. 30, 2018</b>	<b>June 30, 2018</b>	<b>Mar 31, 2018</b>	<b>Dec. 31, 2017</b>	<b>Sept. 30, 2017</b>	<b>June 30, 2017</b>	<b>Mar 31, 2017</b>
<b>Statements of Operations Data:</b>								
Product revenue	\$ 504	\$ 498	\$ 648	\$ 340	\$ 487	\$ 523	\$ 438	\$ 475
Revenue	504	498	648	340	487	523	438	475
Loss from operations	(17,283)	(14,816)	(13,564)	(13,455)	(12,716)	(15,196)	(18,339)	(15,672)
Net loss	(17,399)	(15,010)	(13,804)	(13,765)	(13,102)	(15,567)	(18,694)	(16,023)
Basic and diluted net loss per common share	\$ (0.42)	\$ (0.38)	\$ (0.37)	\$ (0.40)	\$ (0.44)	\$ (0.54)	\$ (0.64)	\$ (0.58)

### 19. 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, 2019, 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, 2019, the number of shares available for issuance under the ESPP increased by 207,402.

The Company sold an additional 1,318,481 shares of common stock between January 1, 2019 and February 22, 2019, at-the-market under the 2016 Sales Agreement discussed in Note 10, resulting in net proceeds of approximately \$4,967 after underwriting discounts, commissions and expenses. As of February 25, 2019, the Company had nothing 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.

#### *Private Placement of Convertible Debt*

In March 2019, the Company entered into a Note Purchase Agreement (the “Purchase Agreement”), with Cap 1 LLC, (the “Purchaser”) an affiliate of Summer Road LLC, to issue and sell to the Purchaser unsecured senior subordinated convertible notes, (“the Notes”), in the original aggregate principal amount of \$37.5 million within five business days of the Agreement Date or upon such later date as mutually agreed between the Company and the Purchaser in writing (such date, the “Closing Date”). In accordance with the Purchase Agreement, each Note accrues interest at a rate of 6% of its outstanding principal amount per annum, payable at maturity. The maturity date of each Note is March 1, 2026, unless earlier converted, repurchased or redeemed as described below.

Holders may, subject to certain conditions, convert all or part of the outstanding principal amount of their Notes into shares of the Company’s common stock, par value \$0.0001 per share, or the 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 conversion rate for the Notes will initially be 153.8462 shares of the Company’s common stock per \$1,000 principal amount of the Notes, which is equivalent to an initial conversion price of approximately \$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 in a combination thereof. Upon any conversion of any Note, the Company is obligated to make a cash payment to the holder of such Note for any interest accrued but unpaid on the principal amount converted. Upon the occurrence of a Corporate Transaction (as defined in the Notes), the holder of a Note is entitled, at such holder’s option, to convert all of the outstanding principal amount of the Note in accordance with the foregoing and receive an additional, “make-whole” cash payment in accordance with a table set forth in each Note.

Upon the occurrence of a Corporate Transaction, each holder of a Note 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 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), the Company is entitled, at its option, to redeem all or part of the outstanding principal amount of the Notes, on a pro rata basis, at an optional redemption price equal to 100% of the outstanding principal amount of the 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 the Company and the Purchaser. The Purchase Agreement does not include any financial covenants. The Company’s obligations under the Purchase Agreement and the 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 Common Stock.

In connection with the execution of the Purchase Agreement and the issuance and sale of the Notes thereunder, the Company and the Purchaser have agreed to enter into a registration rights agreement on the Closing Date, (the “Registration Rights Agreement”). Under the terms of the Registration Rights Agreement and subject to specified exceptions, the Company will be obligated to use commercially reasonable efforts, at its expense, to file a resale registration statement (the “Registration Statement”) with the SEC to register the Common Stock underlying the Notes within 30 days of the Closing Date and to have the SEC declare the Registration Statement effective within 90 days of the Closing Date. The Company will be further obligated to use commercially reasonable efforts to cause the Registration Statement to remain continuously effective until the earlier of the dates when all securities registrable under the Registration Rights Agreement (i) have been sold or (ii) may be sold without restriction, subject to certain conditions, pursuant to Rule 144 promulgated under the Securities Act of 1993, as amended.

#### *Amendment to Existing 2018 Amended Credit Facility*

In accordance with the 2018 Amended Credit Facility, in connection with the Company’s desire to enter into the Purchase Agreement and issue and sell the Notes thereunder, the Company, MidCap, and the Senior Lenders entered into an amendment to the 2018 Amended Credit Facility (“Subsequent Amendment”) on February 21, 2019 (the “Agreement Date”). The Subsequent Amendment added to the 2018 Amended Credit Facility, among other provisions, a negative covenant restricting the Company from paying the holders of the Notes ahead in priority to the Senior 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 also constituted an event of default under the Credit Agreement.

*Subordination Agreement*

In connection with the execution of the Subsequent Amendment, the Company; Cap 1, for itself and on behalf of any future holder of the Notes, or collectively, the Subordinated Creditors; and MidCap, as agent for the Senior Lenders, entered a subordination agreement on the Agreement Date (the "Subordination Agreement"). Under the terms of the Subordination Agreement, as an inducement to the Senior Lenders to permit the issuance and sale of the Notes, the Senior Lenders and the Subordinated Creditors agreed that the Notes are subordinate to the Credit Facility and that any and all payments to the holders of the Notes are subject to the payment in full of the Credit Facility. Until the Credit Facility is paid in full, as defined in the Subordination Agreement, the Subordinated Creditors agree not to take any enforcement action, as defined in the Subordination Agreement, with respect to all or any portion of the Notes, without the prior written consent of the agent for the Senior Lenders.

**REGISTRATION RIGHTS AGREEMENT**

This REGISTRATION RIGHTS AGREEMENT (this “Agreement”) is made and entered into as of March 1, 2019 by and among Ocular Therapeutix, Inc., a Delaware corporation (the “Company”), and the “Purchasers” named in that certain Note Purchase Agreement by and among the Company and the Purchasers dated as of February 21, 2019 (the “Purchase Agreement”). Capitalized terms used herein have the respective meanings ascribed thereto in the Purchase Agreement unless otherwise defined herein.

The parties hereby agree as follows:

1. Certain Definitions.

As used in this Agreement, the following terms shall have the following meanings:

“Closing Date” means the date of the purchase and sale of the Notes pursuant to the Purchase Agreement.

“Common Stock” means the common stock, \$0.0001 par value per share, of the Company.

“Conversion Shares” means shares of Common Stock issued or issuable upon the conversion of the Notes.

“Exchange Act” means the Securities Exchange Act of 1934, as amended, including the rules and regulations promulgated thereunder.

“Note” or “Notes” means senior subordinated convertible notes issued by the Company pursuant to the Purchase Agreement.

“Purchasers” means (i) the Purchasers identified in the Purchase Agreement and (ii) any permitted transferee of any Purchaser who is a subsequent holder of Registrable Securities.

“Prospectus” means (i) the prospectus included in any Registration Statement, as amended or supplemented by any prospectus supplement, with respect to the terms of the offering of any portion of the Registrable Securities covered by such Registration Statement and by all other amendments and supplements to the prospectus, including post-effective amendments and all material incorporated by reference in such prospectus, and (ii) any “free writing prospectus” as defined in Rule 405 under the Securities Act.

“Register,” “registered” and “registration” refer to a registration made by preparing and filing a Registration Statement or similar document in compliance with the Securities Act, and the declaration or ordering of effectiveness of such Registration Statement or document.

“Registrable Securities” means (i) the Conversion Shares, (ii) the shares of Common Stock set forth on Schedule A hereto and (iii) any other securities issued or issuable with respect to or in exchange for Conversion Shares or the shares of Common Stock set forth on Schedule A, whether by merger, charter amendment or otherwise; provided that a security shall cease to be a Registrable Security upon the earlier of (A) a sale pursuant to a Registration Statement or a valid exemption

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under the Securities Act, and (B) such security becoming eligible for sale without restriction by the Purchasers pursuant to Rule 144 and without the requirement to be in compliance with Rule 144(c)(1) (or any successor thereto) promulgated under the Securities Act.

“Registration Statement” means any registration statement of the Company under the Securities Act that covers the resale of any of the Registrable Securities pursuant to the provisions of this Agreement, amendments and supplements to such Registration Statement, including post-effective amendments, all exhibits and all material incorporated by reference in such Registration Statement.

“Required Purchasers” means the Purchaser (or Purchasers) holding a majority of the issued or issuable Registrable Securities.

“SEC” means the U.S. Securities and Exchange Commission.

“Securities Act” means the Securities Act of 1933, as amended, including the rules and regulations promulgated thereunder.

“Selling Securityholder Questionnaire” means a form of selling securityholder questionnaire as may be reasonably requested by the Company from time to time.

## 2. Registration.

(a) Registration Statement. The Company shall use commercially reasonable efforts to (i) promptly prepare and file with the SEC one Registration Statement covering the resale of all of the Registrable Securities within thirty (30) days after the Closing Date (the “Filing Deadline”) and (ii) make such Registration Statement become effective with the SEC within ninety (90) days after the Closing Date (or as soon as practicable thereafter). Subject to any SEC comments, such Registration Statement shall include the plan of distribution attached hereto as Exhibit A; provided, however, that no Purchaser shall be named as an “underwriter” in such Registration Statement without the Purchaser’s prior written consent. Such Registration Statement also shall cover, to the extent allowable under the Securities Act and the rules promulgated thereunder (including Rule 416), such indeterminate number of additional shares of Common Stock resulting from stock splits, stock dividends or similar transactions with respect to the Registrable Securities. Such Registration Statement (and each amendment or supplement thereto, and each request for acceleration of effectiveness thereof) shall be provided in accordance with Section 3(c) hereof to the Purchasers prior to its filing or other submission.

(b) Expenses. The Company will pay all expenses associated with each Registration Statement, including filing and printing fees, the Company’s counsel and accounting fees and expenses, costs associated with clearing the Registrable Securities for sale under applicable state securities laws and listing fees, but excluding discounts, commissions, fees of underwriters, selling brokers, dealer managers or similar securities industry professionals with respect to the Registrable Securities being sold.

(c) Effectiveness.

(i) The Company shall use commercially reasonable efforts to have each Registration Statement declared effective as soon as practicable. The Company shall notify the Purchasers by facsimile or e-mail as promptly as practicable, and in any event, within twenty-four (24) hours, after any Registration Statement is declared effective and shall simultaneously provide the Purchasers with copies of any related Prospectus to be used in connection with the sale or other disposition of the securities covered thereby.

(ii) For not more than sixty (60) consecutive days or for a total of not more than one hundred twenty (120) days in any twelve (12) month period, the Company may suspend the use of any Prospectus included in any Registration Statement contemplated by this Section 2 in the event that the Company determines in good faith that such suspension is necessary to (A) delay the disclosure of material non-public information concerning the Company, the disclosure of which at the time is not, in the good faith opinion of the Company, in the best interests of the Company, (B) amend or supplement the affected Registration Statement or the related Prospectus so that such Registration Statement or Prospectus shall not include an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein, in the case of the Prospectus in light of the circumstances under which they were made, not misleading, (C) permit the Company to conduct a sale of securities or other financing that is not a sale of Registrable Securities or (D) file a replacement Registration Statement covering the resale of Registrable Securities in connection with the expiration or anticipated expiration of an effective Registration Statement (an “Allowed Delay”); provided that the Company shall promptly (a) notify each Purchaser in writing of the commencement of an Allowed Delay, but shall not (without the prior written consent of an Purchaser) disclose to such Purchaser any material non-public information giving rise to an Allowed Delay, (b) advise the Purchasers in writing to cease all sales under such Registration Statement until the end of the Allowed Delay and (c) use commercially reasonable efforts to terminate an Allowed Delay as promptly as practicable.

(d) Rule 415; Cutback. If at any time the SEC takes the position that the offering of some or all of the Registrable Securities in a Registration Statement is not eligible to be made on a delayed or continuous basis under the provisions of Rule 415 under the Securities Act or requires any Purchaser to be named as an “underwriter,” the Company shall use commercially reasonable efforts to persuade the SEC that the offering contemplated by such Registration Statement is a valid secondary offering and not an offering “by or on behalf of the issuer” as defined in Rule 415 and that none of the Purchasers is an “underwriter.” The Purchasers shall have the right to select one legal counsel to review and oversee any registration or matters pursuant to this Section 2(d), including participation in any meetings or discussions with the SEC regarding the SEC’s position and to comment on any written submission made to the SEC with respect thereto, which counsel shall be designated by the Required Purchasers. In the event that, despite the Company’s commercially reasonable efforts and compliance with the terms of this Section 2(d), the SEC does not alter its position, the Company shall (i) remove from such Registration Statement such portion of the Registrable Securities (the “Cut Back Shares”) and/or (ii) agree to such restrictions and limitations on the registration and resale of the Registrable Securities as the SEC may require to assure the Company’s compliance with the requirements of Rule 415 (collectively, the “SEC Restrictions”); provided, however, that the Company shall not agree to name any Purchaser as an “underwriter” in such Registration Statement without the prior written consent of such Purchaser. Any cut-back imposed on the Purchasers pursuant to this

Section 2(d) shall be allocated among the Purchasers on a pro rata basis and shall be applied first to any of the Registrable Securities of such Purchaser as such Purchaser shall designate, unless the SEC Restrictions otherwise require or provide or the Purchasers otherwise agree. From and after such date as the Company is able to effect the registration of such Cut Back Shares, the Company shall use commercially reasonable efforts to file a Registration Statement relating to such Cut Back Shares and to have such Registration Statement declared effective by the SEC.

3. Company Obligations. The Company will use commercially reasonable efforts to effect the registration of the Registrable Securities in accordance with the terms hereof, and pursuant thereto the Company will, as expeditiously as possible:

(a) use commercially reasonable efforts to cause such Registration Statement to remain continuously effective for a period that will terminate upon the earlier of (i) the date on which all Registrable Securities covered by such Registration Statement as amended from time to time, and actually issued or issuable upon conversion of the Notes have been sold and (ii) the date on which all Registrable Securities covered by such Registration Statement and actually issued or issuable upon conversion of the Notes may be sold without restriction pursuant to Rule 144 and without the requirement to be in compliance with Rule 144(c)(1) (or any successor thereto) promulgated under the Securities Act (the "Effectiveness Period"), and advise the Purchasers promptly in writing when the Effectiveness Period has expired;

(b) use commercially reasonable efforts to prepare and file with the SEC such amendments and post-effective amendments to such Registration Statement and the related Prospectus as may be necessary to keep such Registration Statement effective for the Effectiveness Period and to comply with the provisions of the Securities Act and the Exchange Act with respect to the distribution of all of the Registrable Securities covered thereby;

(c) provide copies to and permit any counsel designated by the Purchasers to review each Registration Statement and all amendments and supplements thereto (but excluding any documents incorporated by reference in such Registration Statement, amendments or supplements that are available on the SEC's Electronic Data Gathering, Analysis, and Retrieval system (or any successor system)) no fewer than three (3) Business Days prior to their filing with the SEC and not file any document to which such counsel reasonably objects;

(d) furnish to each Purchaser whose Registrable Securities are included in any Registration Statement (i) promptly after the same is prepared and filed with the SEC, if requested by the Purchaser, one (1) copy of any Registration Statement and any amendment thereto, each preliminary prospectus and Prospectus and each amendment or supplement thereto, and each letter written by or on behalf of the Company to the SEC or the staff of the SEC, and each item of correspondence from the SEC or the staff of the SEC, in each case relating to such Registration Statement (other than any portion of any of the foregoing which contains information for which the Company has sought confidential treatment), and (ii) such number of copies of a Prospectus, including a preliminary prospectus, and all amendments and supplements thereto and such other documents as each Purchaser may reasonably request in order to facilitate the disposition of the Registrable Securities owned by such Purchaser that are covered by such Registration Statement;

(e) use commercially reasonable efforts to (i) prevent the issuance of any stop order or other suspension of effectiveness and, (ii) if such order is issued, obtain the withdrawal of any such order at the earliest practical moment;

(f) prior to any public offering of Registrable Securities, use commercially reasonable efforts to register or qualify or cooperate with the Purchasers and their counsel in connection with the registration or qualification of such Registrable Securities for the offer and sale under the securities or blue sky laws of such jurisdictions requested by the Purchasers and do any and all other commercially reasonable acts or things necessary or advisable to enable the distribution in such jurisdictions of the Registrable Securities covered by the Registration Statement; provided, however, that the Company shall not be required in connection therewith or as a condition thereto to (i) qualify to do business in any jurisdiction where it would not otherwise be required to qualify but for this Section 3(f), (ii) subject itself to general taxation in any jurisdiction where it would not otherwise be so subject but for this Section 3(f), or (iii) file a general consent to service of process in any such jurisdiction;

(g) use commercially reasonable efforts to cause all Registrable Securities covered by a Registration Statement to be listed on each securities exchange, interdealer quotation system or other market on which similar securities issued by the Company are then listed;

(h) promptly notify the Purchasers, at any time prior to the end of the Effectiveness Period, upon discovery that, or upon the happening of any event as a result of which, the Prospectus includes an untrue statement of a material fact or omits to state any material fact required to be stated therein or necessary to make the statements therein not misleading in light of the circumstances then existing, and promptly prepare, file with the SEC and furnish to such holder a supplement to or an amendment of such Prospectus as may be necessary so that such Prospectus shall not include an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading in light of the circumstances then existing;

(i) otherwise use commercially reasonable efforts to comply with all applicable rules and regulations of the SEC under the Securities Act and the Exchange Act, including, without limitation, Rule 172 under the Securities Act, file any final Prospectus, including any supplement or amendment thereof, with the SEC pursuant to Rule 424 under the Securities Act, promptly inform the Purchasers in writing if, at any time during the Effectiveness Period, the Company does not satisfy the conditions specified in Rule 172 and, as a result thereof, the Purchasers are required to deliver a Prospectus in connection with any disposition of Registrable Securities and take such other actions as may be reasonably necessary to facilitate the registration of the Registrable Securities hereunder; and make available to its security holders, as soon as reasonably practicable, an earnings statement covering a period of at least twelve (12) months, beginning after the effective date of each Registration Statement, which earnings statement shall satisfy the provisions of Section 11(a) of the Securities Act, including Rule 158 promulgated thereunder; and

(j) with a view to making available to the Purchasers the benefits of Rule 144 (or its successor rule) and any other rule or regulation of the SEC that may at any time permit the Purchasers to sell shares of Common Stock to the public without registration, the Company covenants and agrees to: (i) make and keep public information available, as those terms are

understood and defined in Rule 144, until the earlier of (A) six months after such date as all of the Registrable Securities may be sold without restriction by the holders thereof pursuant to Rule 144 and without the requirement to be in compliance with Rule 144(c)(1) (or any successor thereto) promulgated under the Securities Act or any other rule of similar effect or (B) such date as all of the Registrable Securities shall have been resold; (ii) file with the SEC in a timely manner all reports and other documents required of the Company under the Exchange Act; and (iii) furnish to each Purchaser upon request, as long as such Purchaser owns any Registrable Securities, (A) a written statement by the Company that it has complied with the reporting requirements of the Exchange Act, (B) a copy of the Company's most recent Annual Report on Form 10-K or Quarterly Report on Form 10-Q, and (C) such other information as may be reasonably requested in order to avail such Purchaser of any rule or regulation of the SEC that permits the selling of any such Registrable Securities without registration.

Notwithstanding the foregoing, it is understood and agreed that a Registration Statement may expire pursuant to the rules and regulations of the SEC on the date that is three years following the date it is declared effective by the SEC and that in such case either prior to or promptly following such expiration time, the Company agrees to use commercially reasonable efforts to prepare, file and caused to be declared effective a replacement Registration Statement. It is agreed that the expiration of a Registration Statement pursuant to the rules and regulations of the SEC shall not represent a violation or breach of any of the Company's obligations under this Agreement; provided that in such case the Company uses commercially reasonable efforts to file and caused to be declared effective a replacement Registration Statement.

#### 4. Obligations of the Purchasers.

(a) It shall be a condition precedent to the obligations of the Company to take any action pursuant to Section 2 hereof with respect to the Registrable Securities of any Purchaser that such Purchaser furnish in writing to the Company a Selling Securityholder Questionnaire and any other information regarding itself, the Registrable Securities held by it and the intended method of disposition of the Registrable Securities held by it, as shall be reasonably required to effect the registration of such Registrable Securities, and such Purchaser shall execute such documents in connection with such registration as the Company may reasonably request. At least five (5) Business Days prior to the first anticipated filing date of any Registration Statement, the Company shall notify each Purchaser of the information the Company requires from such Purchaser if such Purchaser elects to have any of the Registrable Securities included in such Registration Statement. A Purchaser shall provide such information to the Company at least two (2) Business Days prior to the first anticipated filing date of such Registration Statement if such Purchaser elects to have any of the Registrable Securities included in such Registration Statement.

(b) Each Purchaser, by its acceptance of the Registrable Securities, agrees to cooperate with the Company as reasonably requested by the Company in connection with the preparation and filing of a Registration Statement hereunder, unless such Purchaser has notified the Company in writing of its election to exclude all of its Registrable Securities from such Registration Statement.

(c) Each Purchaser agrees that, upon receipt of any notice from the Company of either (i) the commencement of an Allowed Delay pursuant to Section 2(c)(ii) or (ii) the

happening of an event pursuant to Section 3(h) hereof, such Purchaser will immediately discontinue disposition of Registrable Securities pursuant to any Registration Statement covering such Registrable Securities, until the Purchaser is advised by the Company that such dispositions may again be made.

(d) Each Purchaser covenants and agrees that it will comply with the prospectus delivery requirements of the Securities Act as applicable to it or an exemption therefrom in connection with sales of Registrable Securities pursuant to any Registration Statement.

(e) The Purchaser listed on Schedule A hereto represents that the number of shares opposite its name is the total number of shares of Common Stock beneficially owned by such Purchaser as of the date of this Agreement.

5. Indemnification.

(a) Indemnification by the Company. The Company will indemnify and hold harmless each Purchaser and its officers, directors, members, employees and agents, successors and assigns, and each other person, if any, who controls such Purchaser within the meaning of the Securities Act, against any losses, claims, damages or liabilities, joint or several, to which they may become subject under the Securities Act or otherwise, insofar as such losses, claims, damages or liabilities (or actions in respect thereof) arise out of or are based upon: (i) any untrue statement or alleged untrue statement or omission or alleged omission of any material fact contained in any Registration Statement, any preliminary Prospectus or final Prospectus, or any amendment or supplement thereof; (ii) any violation by the Company or its agents of any rule or regulation promulgated under the Securities Act applicable to the Company or its agents and relating to action or inaction required of the Company in connection with such registration; or (iii) any failure to register or qualify the Registrable Securities included in any such Registration Statement in any state where the Company or its agents has affirmatively undertaken or agreed in writing that the Company will undertake such registration or qualification on an Purchaser's behalf and will reimburse such Purchaser, and each such officer, director or member and each such controlling person for any legal or other expenses reasonably incurred by them in connection with investigating or defending any such loss, claim, damage, liability or action; provided, however, that the Company will not be liable in any such case if and to the extent that any such loss, claim, damage or liability arises out of or is based upon (i) an untrue statement or alleged untrue statement or omission or alleged omission so made in conformity with information furnished by such Purchaser or any such controlling person in writing specifically for use in such Registration Statement or Prospectus, (ii) the use by an Purchaser of an outdated or defective Prospectus after the Company has notified such Purchaser in writing that such Prospectus is outdated or defective, (iii) an Purchaser's failure to send or give a copy of the Prospectus or supplement (as then amended or supplemented), if required (and not exempted) to the Persons asserting an untrue statement or omission or alleged untrue statement or omission at or prior to the written confirmation of the sale of Registrable Securities or (iv) the disposition of any Registrable Securities pursuant to any Registration Statement or Prospectus covering such Registrable Securities during an Allowed Delay.

(b) Indemnification by the Purchasers. Each Purchaser agrees, severally but not jointly, to indemnify and hold harmless, to the fullest extent permitted by law, the Company,

its directors, officers, employees, stockholders and each person who controls the Company (within the meaning of the Securities Act) against any losses, claims, damages, liabilities and expense (including reasonable attorney fees) resulting from any untrue statement of a material fact or any omission of a material fact required to be stated in any Registration Statement or Prospectus or preliminary Prospectus or amendment or supplement thereto or necessary to make the statements therein not misleading, to the extent, but only to the extent that such untrue statement or omission is contained in any information furnished in writing by such Purchaser to the Company specifically for inclusion in such Registration Statement or Prospectus or amendment or supplement thereto. Except to the extent that any such losses claims, damages, liabilities or expenses are finally judicially determined to have resulted from a Purchaser's fraud or willful misconduct, in no event shall the liability of an Purchaser be greater in amount than the dollar amount of the proceeds (net of all expense paid by such Purchaser in connection with any claim relating to this Section 5 and the amount of any damages such Purchaser has otherwise been required to pay by reason of such untrue statement or omission) received by such Purchaser upon the sale of the Registrable Securities included in such Registration Statement giving rise to such indemnification obligation.

(c) Conduct of Indemnification Proceedings. Any person entitled to indemnification hereunder shall (i) give prompt notice to the indemnifying party of any claim with respect to which it seeks indemnification and (ii) permit such indemnifying party to assume the defense of such claim with counsel reasonably satisfactory to the indemnified party; provided that any person entitled to indemnification hereunder shall have the right to employ separate counsel and to participate in the defense of such claim, but the fees and expenses of such counsel shall be at the expense of such person unless (a) the indemnifying party has agreed to pay such fees or expenses, (b) the indemnifying party shall have failed to assume the defense of such claim and employ counsel reasonably satisfactory to such person or (c) in the reasonable judgment of any such person, based upon written advice of its counsel, a conflict of interest exists between such person and the indemnifying party with respect to such claims (in which case, if the person notifies the indemnifying party in writing that such person elects to employ separate counsel at the expense of the indemnifying party, the indemnifying party shall not have the right to assume the defense of such claim on behalf of such person); and provided, further, that the failure of any indemnified party to give notice as provided herein shall not relieve the indemnifying party of its obligations hereunder, except to the extent that such failure to give notice shall materially adversely affect the indemnifying party in the defense of any such claim or litigation. It is understood that the indemnifying party shall not, in connection with any proceeding in the same jurisdiction, be liable for fees or expenses of more than one separate firm of attorneys at any time for all such indemnified parties. No indemnifying party will, except with the consent of the indemnified party, which shall not be unreasonably withheld or conditioned, consent to entry of any judgment or enter into any settlement that does not include as an unconditional term thereof the giving by the claimant or plaintiff to such indemnified party of a release from all liability in respect of such claim or litigation.

(d) Contribution. If for any reason the indemnification provided for in the preceding paragraphs (a) and (b) is unavailable to an indemnified party or insufficient to hold it harmless, other than as expressly specified therein, then the indemnifying party shall contribute to the amount paid or payable by the indemnified party as a result of such loss, claim, damage or liability in such proportion as is appropriate to reflect the relative fault of the indemnified party and the indemnifying party, as well as any other relevant equitable considerations. No person

guilty of fraudulent misrepresentation within the meaning of Section 11(f) of the Securities Act shall be entitled to contribution from any person not guilty of such fraudulent misrepresentation. Except to the extent that any such losses claims, damages, liabilities or expenses are finally judicially determined to have resulted from a holder of Registrable Securities' fraud or willful misconduct, in no event shall the contribution obligation of a holder of Registrable Securities be greater in amount than the dollar amount of the proceeds (net of all expenses paid by such holder in connection with any claim relating to this Section 5 and the amount of any damages such holder has otherwise been required to pay by reason of such untrue or alleged untrue statement or omission or alleged omission) received by it upon the sale of the Registrable Securities giving rise to such contribution obligation.

6. Miscellaneous.

(a) Amendments and Waivers. This Agreement may be amended only by a writing signed by the Company and the Required Purchasers. The Company may take any action herein prohibited, or omit to perform any act herein required to be performed by it, only if the Company shall have obtained the written consent to such amendment, action or omission to act of the Required Purchasers.

(b) Notices. All notices and other communications provided for or permitted hereunder shall be made as set forth in Section 6.1 of the Purchase Agreement.

(c) Assignments and Transfers by Purchasers. The provisions of this Agreement shall be binding upon and inure to the benefit of the Purchasers and their respective successors and assigns. A Purchaser may transfer or assign, in whole or from time to time in part, to one or more persons its rights hereunder in connection with the transfer of Registrable Securities by such Purchaser to such person, provided that such Purchaser complies with all laws applicable thereto and the provisions of the Purchase Agreement and the Notes, and provides written notice of assignment to the Company promptly after such assignment is effected, and such person agrees in writing to be bound by all of the provisions contained herein.

(d) Assignments and Transfers by the Company. This Agreement may not be assigned by the Company (whether by operation of law or otherwise) without the prior written consent of the Required Purchasers; provided, however, that in the event that the Company is a party to a merger, consolidation, share exchange or similar business combination transaction in which the Common Stock is converted into the equity securities of another Person, from and after the effective time of such transaction, such Person shall, by virtue of such transaction, be deemed to have assumed the obligations of the Company hereunder, the term "Company" shall be deemed to refer to such Person and the term "Registrable Securities" shall be deemed to include the securities received by the Purchasers in connection with such transaction unless such securities are otherwise freely tradable by the Purchasers after giving effect to such transaction.

(e) Benefits of the Agreement. The terms and conditions of this Agreement shall inure to the benefit of and be binding upon the respective permitted successors and assigns of the parties. Nothing in this Agreement, express or implied, is intended to confer upon any party other than the parties hereto or their respective successors and assigns any rights, remedies,

obligations, or liabilities under or by reason of this Agreement, except as expressly provided in this Agreement.

(f) Counterparts. This Agreement may be executed in several counterparts, and by each Party on separate counterparts, each of which and any photocopies or other electronic transmission (including by PDF) thereof shall be deemed an original, but all of which together shall constitute one and the same agreement.

(g) Titles and Subtitles. The titles and subtitles used in this Agreement are used for convenience only and are not to be considered in construing or interpreting this Agreement.

(h) Severability. Any provision of this Agreement that is prohibited or unenforceable in any jurisdiction shall, as to such jurisdiction, be ineffective to the extent of such prohibition or unenforceability without invalidating the remaining provisions hereof but shall be interpreted as if it were written so as to be enforceable to the maximum extent permitted by applicable law, and any such prohibition or unenforceability in any jurisdiction shall not invalidate or render unenforceable such provision in any other jurisdiction. To the extent permitted by applicable law, the parties hereby waive any provision of law which renders any provisions hereof prohibited or unenforceable in any respect.

(i) Further Assurances. The parties shall execute and deliver all such further instruments and documents and take all such other actions as may reasonably be required to carry out the transactions contemplated hereby and to evidence the fulfillment of the agreements herein contained.

(j) Entire Agreement. This Agreement is intended by the parties as a final expression of their agreement and intended to be a complete and exclusive statement of the agreement and understanding of the parties hereto in respect of the subject matter contained herein. This Agreement supersedes all prior agreements and understandings between the parties with respect to such subject matter.

(k) Governing Law; Consent to Jurisdiction; Waiver of Jury Trial. All questions concerning the construction, validity, enforcement and interpretation of this Agreement shall be governed by and construed and enforced in accordance with the internal laws of the State of New York without regard to the choice of law principles thereof. Each Party agrees that all legal proceedings concerning the interpretations, enforcement and defense of the transactions contemplated by this Agreement (whether brought against a Party hereto or its respective Affiliates, directors, officers, shareholders, employees or agents) shall be commenced exclusively in the state and federal courts sitting in the City of New York. Each Party hereby irrevocably submits to the exclusive jurisdiction of the state and federal courts sitting in the City of New York, borough of Manhattan for the adjudication of any dispute hereunder or in connection herewith or with any transaction contemplated hereby or discussed herein, and hereby irrevocably waives, and agrees not to assert in any suit, action or other proceeding, any claim that it is not personally subject to the jurisdiction of any such court, that such suit, action or proceeding is improper or is an inconvenient venue for such proceeding. Each Party hereby irrevocably waives personal service of process and consents to process being served in any such suit, action or other proceeding by mailing a copy thereof via registered or certified United States mail or overnight delivery (with

evidence of delivery) to such Party at the address in effect for notices to it under this Agreement and agrees that such service shall constitute good and sufficient service of process and notice thereof. Nothing contained herein shall be deemed to limit in any way any right to serve process in any other manner permitted by law. THE PARTIES HEREBY WAIVE ALL RIGHTS TO A TRIAL BY JURY.

[remainder of page intentionally left blank]

IN WITNESS WHEREOF, the parties have executed this Agreement or caused their duly authorized officers to execute this Agreement as of the date first above written.

COMPANY:

OCULAR THERAPEUTIX, INC.

By: /s/ Donald Notman  
Name: Donald Notman  
Title: Chief Financial Officer

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**PURCHASERS:**

**CAP 1 LLC**

By: /s/ Stephen A. Ives

Name: Stephen A. Ives

Title: Vice President

Address:

c/o Summer Road LLC

655 Madison Avenue, 19th Floor

New York, New York 10065

Attn: Richard A. Silberberg, *Chief Operating Officer*

Email:

With a copy to:

Norton Rose Fulbright US LLP

1301 Avenue of the Americas

New York, New York 10019-6022

Attn: Frank S. Vellucci, Esq.

Email: [frank.vellucci@nortonrosefulbright.com](mailto:frank.vellucci@nortonrosefulbright.com)

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<b>Purchaser</b>	<b>Additional Registrable Securities</b>
Cap 1 LLC	3,804,788 shares of Common Stock

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### Plan of Distribution

The selling stockholders, which as used herein includes donees, pledgees, transferees or other successors-in-interest selling shares of common stock or interests in shares of common stock received after the date of this prospectus from a selling stockholder as a gift, pledge, partnership distribution or other transfer, may, from time to time, sell, transfer or otherwise dispose of any or all of their shares of common stock or interests in shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices.

The selling stockholders may use any one or more of the following methods when disposing of shares or interests therein:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales effected after the date the registration statement of which this prospectus is a part is declared effective by the SEC;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted by applicable law.

The selling stockholders may, from time to time, pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock, from time to time, under this prospectus, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act of 1933, as amended (the “Securities Act”), amending the list of selling stockholders to include the pledgee, transferee or

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other successors in interest as selling stockholders under this prospectus. The selling stockholders also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of common stock or interests therein, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the common stock in the course of hedging the positions they assume. The selling stockholders may also sell shares of common stock short and deliver these securities to close out their short positions, or loan or pledge the common stock to broker-dealers that in turn may sell these securities. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The aggregate proceeds to the selling stockholders from the sale of the common stock offered by them will be the purchase price of the common stock less discounts or commissions, if any. Each of the selling stockholders reserves the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of common stock to be made directly or through agents. We will not receive any of the proceeds from this offering.

The selling stockholders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act, provided that they meet the criteria and conform to the requirements of that rule.

The selling stockholders and any underwriters, broker-dealers or agents that participate in the sale of the common stock or interests therein may be “underwriters” within the meaning of Section 2(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the shares may be underwriting discounts and commissions under the Securities Act. Selling stockholders who are “underwriters” within the meaning of Section 2(11) of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act.

To the extent required, the shares of our common stock to be sold, the names of the selling stockholders, the respective purchase prices and public offering prices, the names of any agents, dealer or underwriter, and any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the common stock may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the common stock may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have advised the selling stockholders that the anti-manipulation rules of Regulation M promulgated under the Securities Exchange Act of 1934, as amended, may apply to sales of shares

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in the market and to the activities of the selling stockholders and their affiliates. In addition, to the extent applicable we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling stockholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling stockholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

We have agreed to indemnify the selling stockholders against liabilities, including liabilities under the Securities Act and state securities laws, relating to the registration of the shares offered by this prospectus.

We have agreed with the selling stockholders to keep the registration statement of which this prospectus constitutes a part effective until the earlier of (1) such time as all of the shares covered by this prospectus and actually issued or issuable upon conversion of the Notes have been sold and (2) the date on which all of the shares may be sold without restriction pursuant to Rule 144 of the Securities Act.

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CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (Nos. 333-210777 and 333-229085) and Form S-8 (Nos. 333-198240, 333-202886, 333-210059, 333-216622 and 333-223513) of Ocular Therapeutix, Inc. of our report dated March 7, 2019 relating to the financial statements, which appears in this Form 10-K.

/s/PricewaterhouseCoopers LLP  
Boston, Massachusetts  
March 7, 2019

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## 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 7, 2019

By: /s/ Antony Mattessich  
Antony Mattessich  
President and Chief Executive Officer  
(Principal Executive Officer)

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## 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 7, 2019

By: /s/ Donald Notman  
Donald Notman  
Chief Financial Officer  
(Principal Financial and Accounting Officer)

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**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, 2018 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 7, 2019

By: /s/ Antony Mattessich

Antony Mattessich  
President and Chief Executive Officer  
(Principal Executive Officer)

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**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, 2018 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 7, 2019

By: /s/ Donald Notman

Donald Notman

Chief Financial Officer

(Principal Financial and Accounting Officer)

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