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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2017

or

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

For the transition period from_____ to _____

Commission file number 001-36554

Ocular Therapeutix, Inc.

(Exact name of registrant as specified in its charter)

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

(781) 357-4000

(Registrant's telephone number, including area code)

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

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

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

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

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

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate website, if any, every Interactive Data File required to be submitted and posted 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 and post 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	☐	Accelerated filer	☒
Non-accelerated filer	☐ (Do not check if a smaller reporting company) ☐	Smaller reporting company	☐ ☐
		Emerging growth company	☒

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

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

As of June 30, 2017, the aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant was approximately $221 million. The number of shares outstanding of the registrant's class of common stock, as of March 1, 2018: 37,278,082

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report incorporates by reference information from the definitive Proxy Statement for the registrant's 2018 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, 2017.

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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 our product candidates based on our proprietary bioresorbable hydrogel technology platform;
- our plans and ability to resolve the current manufacturing deficiencies cited by the U.S. Food and Drug Administration, or FDA, in order to resubmit our New Drug Application, or NDA, for DEXTENZA™ for the treatment of post-surgical ocular pain;
- our ability to manufacture DEXTENXA in compliance with current Good Manufacturing Practices, or cGMP;
- our plans to raise additional capital, including through equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements, royalty agreements and marketing and distribution arrangements, generally, and to fund the regulatory submission and commercialization of DEXTENXZA, specifically;
- our ongoing and planned clinical trials, including our Phase 3 clinical trial of DEXTENZA for the treatment of allergic conjunctivitis, our Phase 2 clinical trial of DEXTENZA for the treatment of dry eye disease and our Phase 3 clinical trials of OTX-TP for the treatment of glaucoma and ocular hypertension;
- the timing of and our ability to submit applications and obtain and maintain regulatory approvals for DEXTENZA, OTX-TP and our other product candidates;
- our plans to raise additional capital, including through equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and marketing and distribution arrangements;
- our commercialization of ReSure Sealant;
- the potential advantages of 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;
- the preclinical development of our hydrogel formulated with protein-based or small molecule drugs, including tyrosine kinase inhibitors, or TKIs, for the treatment of wet age-related macular degeneration, or 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 estimates regarding the potential market opportunity for DEXTENZA, OTX-TP, ReSure Sealant and our other product candidates;

- our commercialization, marketing and manufacturing plans, capabilities and strategy;
- the costs and timing of manufacturing, sales, marketing, distribution and other commercialization efforts with respect to ReSure Sealant and any additional products, including DEXTENZA, 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;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- the impact of government laws and regulations;
- the outcome of certain legal actions and 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 incorporate FDA approved therapeutic agents, including small molecules and proteins, into our hydrogel technology with the goal of providing extended delivery of drug to the eye. We believe that our extended delivery technology allows us 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 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.

Our lead product candidates are DEXTENZA (dexamethasone insert), for the treatment of post-surgical ocular pain and inflammation, allergic conjunctivitis and dry eye disease, and OTX-TP (travoprost insert), for the reduction of intraocular pressure, or IOP, in patients with glaucoma and ocular hypertension. Both product candidates are extended-delivery, drug-eluting, preservative-free intracanalicular inserts that are placed into the canaliculus through a natural opening called the punctum located in the inner portion of the eyelid near the nose.

We also have in development two programs that are beginning human clinical trials: OTX-TIC, an intracameral travoprost implant for the reduction of IOP in patients with moderate to severe glaucoma and ocular hypertension; and OTX-TKI, a tyrosine kinase inhibitor intravitreal injection by fine gauge needle, delivering a hydrogel-based, anti-angiogenic formulation that releases the therapeutic agent for the treatment of wet AMD. As of February 28, 2018, we have not enrolled a patient in either program's clinical trials. Finally, we continue our 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 our sole commercial product ReSure Sealant, a hydrogel-based 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 clearance from the ocular surface by a variety of mechanisms can create challenges in the successful management of ocular diseases and conditions. 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 eye drop regimens with our innovative extended-delivery, drug-eluting intracanalicular inserts, which we formerly referred to as punctum plugs. Our intracanalicular inserts are designed to release a therapeutic agent to the surface of the eye over an extended period, with either a single administration for acute conditions or a once every several month administration for chronic diseases and conditions. The goal for our intracanalicular insert product candidates is to change the management of many front-of-the-eye diseases and conditions from frequent, pulsed eye drop therapy, characterized by significant variations in drug concentration over time, to longer term, extended delivery of therapeutic agents to improve patient experiences.

DEXTENZA ™ (dexamethasone insert)

Our most advanced product candidate, DEXTENZA, incorporates the FDA-approved corticosteroid dexamethasone as an active pharmaceutical ingredient into a hydrogel-based, drug-eluting intracanalicular insert. In September 2015, we submitted to the FDA an NDA for DEXTENZA for the treatment of post-surgical ocular pain. In July 2016, we received a Complete Response Letter, or CRL, from the FDA regarding our NDA for DEXTENZA. 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. 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. FDA concerns included deficiencies in manufacturing processes and analytical testing related to manufacturing of drug product identified during the pre-NDA approval inspection. We have corresponded with the FDA regarding these inspectional observations and are working to resolve the issues that have been identified. 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 have undertaken in response to the FDA's inspectional observations and as a result of further internal review include upgrades to our manufacturing equipment and updates to our manufacturing processes and quality oversight. These changes are 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. In December 2017, we requested a meeting with the FDA to describe our remediation efforts and NDA resubmission plans and to seek feedback. A meeting was granted in January 2018, and we believe that the preliminary written responses from the FDA to our questions fully addressed our meeting objectives. We decided that the meeting would no longer be necessary because of the completeness of the FDA's response and that the FDA's comments do not require any substantial change in our manufacturing or regulatory plans. As a result, the correspondence with the FDA will represent the official record of that previously scheduled meeting. Subject to satisfactorily addressing the FDA inspectional observations and demonstrating consistency in our commercial stage manufacturing process, we plan to resubmit our NDA for DEXTENZA for the treatment of post-surgical ocular pain in the first half of 2018. Adequate resolution of the outstanding Form 483 inspectional observations and the final decision as to the adequacy of our manufacturing processes are determined by the FDA with input from the Office of Process and Facilities within its Center for Drug Evaluation and Research, or CDER, as part of the NDA review process, and are necessary prior to NDA approval.

If DEXTENZA is approved for marketing, we are considering the potential commercialization options for DEXTENZA in the United States, including building our own highly targeted, key account sales force that would focus on the ambulatory surgical centers responsible for the largest volumes of cataract surgery. We have not reflected the full costs of building of such a sales force in our current operating plan and will need to raise additional capital to support such an effort.

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 are being used to support our NDA for post-surgical ocular pain. Subject to receiving approval for the pain indication, and based on the results from the previous three Phase 3 clinical trials for DEXTNZA, we plan to submit an NDA supplement, or sNDA, for DEXTENZA for the treatment of post-surgical ocular inflammation. We have also 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 are currently considering potential next steps in pursuing the approval for DEXTENZA in the allergic conjunctivitis indication. Finally, DEXTENZA completed a Phase 2 clinical trial for the treatment of dry eye disease, with topline results announced in December 2015.

OTX-TP (travoprost insert)

Our second product candidate, OTX-TP, incorporates travoprost, an FDA-approved prostaglandin analog, or PGA, that reduces elevated IOP as its active pharmaceutical ingredient, into a hydrogel-based, drug-eluting intracanalicular insert. This preservative-free insert is designed to elute drug for up to 90 days. OTX-TP is being developed to lower IOP in patients with mild to moderate 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 Phase 3 clinical trials of OTX-TP in September 2016. We expect our first Phase 3 trial of OTX-TP to enroll approximately 550 patients at 50 sites in the United States. Based on discussions with the FDA, the first Phase 3 clinical trial design will include an OTX-TP treatment arm and a placebo-controlled comparator arm that will use a non-drug eluting hydrogel-based intracanalicular insert. There will not be a requirement for either a timolol comparator or a validation arm. No eye drops, placebo or active, will be administered in either the

OTX-TP treatment arm or the placebo-controlled arm. The primary efficacy endpoint will be 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 have enrolled over 60% of the target patient enrollment for this trial as of February 28, 2018. We expect topline efficacy data from the first Phase 3 clinical trial in the fourth quarter of 2018. We do not intend to initiate the second Phase 3 clinical trial until we receive data from the first Phase 3 clinical trial and may determine to discuss 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 will need to generate six-month (300 patients) and one year (100 patients) safety data during either the first or second Phase 3 clinical trial to support our product registration.

OTX-TIC (travoprost implant)

OTX-TIC (travoprost implant) is our product candidate for the treatment of patients with moderate to severe glaucoma 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 lowering in humans. We initiated a Phase 1 clinical trial outside the United States in the third quarter of 2017 to assess safety and obtain initial efficacy data, but have not enrolled any patients in this clinical trial as of February 28, 2018. The trial is a prospective, single-center study designed to evaluate the safety, efficacy, durability and tolerability of OTX-TIC compared to topical travoprost (eye drops) in up to 20 patients with open-angle glaucoma or ocular hypertension. We submitted an investigational new drug application, or IND, in the first quarter of 2018 and expect to initiate a second Phase 1 trial in the United States in the first half of 2018.

Back-of-the-Eye Programs

We are engaged in the preclinical 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 six month period of a protein-based large molecule or small molecule TKI drug, 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 (tyrosine kinase inhibitor implant)

OTX-TKI *(*tyrosine kinase inhibitor implant) 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. We plan to initiate a Phase 1 clinical trial to begin outside of the United States in the first half of 2018 to assess the safety, durability, and tolerability of OTX-TKI in the posterior segment of the human eye for the treatment of VEGF induced retinal leakage for an extended duration.

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 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. 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 extended-delivery hydrogel in combination with Regeneron's large molecule VEGF-targeting compounds, or Licensed Products.

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, $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

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 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 new areas of the body. If we are to utilize our intellectual property, all of which we currently license from Incept, LLC, or Incept, for applications outside the field of ophthalmology, we will 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.

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.

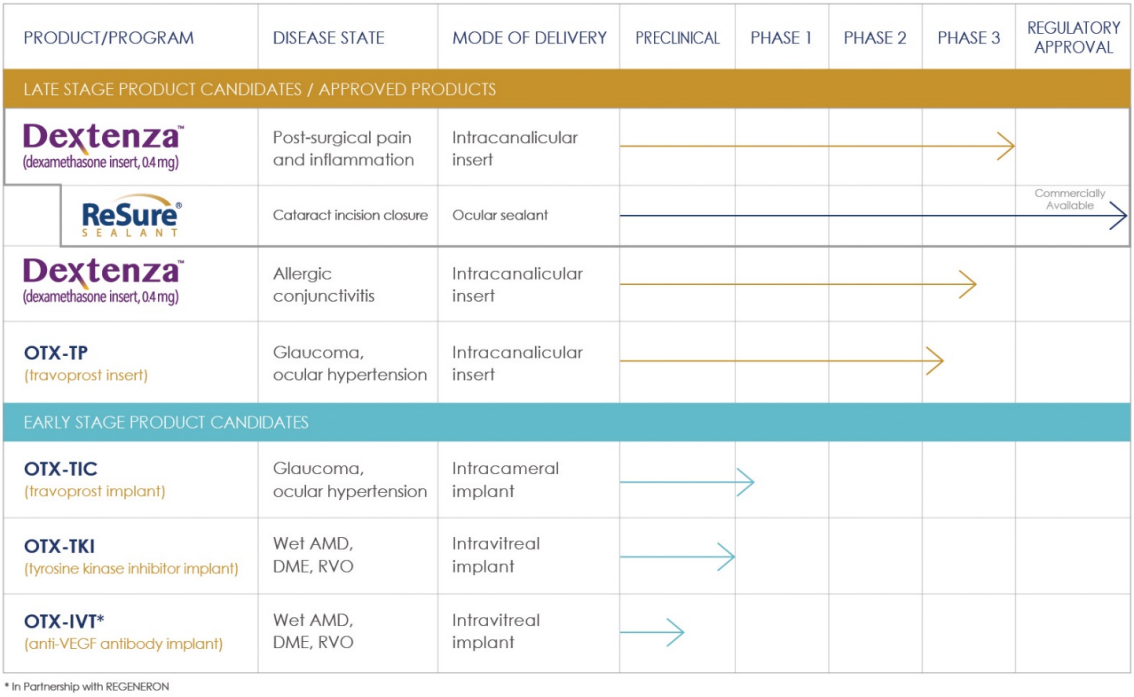
Our product candidates target large and growing markets. Allied Market Research estimates that the annual worldwide market for ophthalmic medications was $29 billion as of 2016 and is expected to increase to $42.7 billion by 2023.

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 Executive Chairman of the Board of Directors, is a general partner of Incept and has a 50% ownership stake in Incept. We are currently in discussions with Incept for the potential expansion of our licensed rights in order to enable our potential use of the technology beyond the field of ophthalmology.

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 for the treatment of retinal diseases.



Our Strategy

Our goal is to change the management of many ophthalmic diseases and conditions from frequent, pulsed therapies, characterized by significant variations in drug concentration over time, to longer term, sustained delivery of therapeutic agents to improve patient experiences. The key elements of our strategy to achieve this goal are to:

- *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 sustained delivery 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.

- *Improve patient compliance and management of front-of-the-eye diseases and conditions by replacing standard of care eye drop therapies with our intracanalicular insert product candidates*. We are designing and developing innovative product candidates to address large markets that are currently served by a variety of competing products, all of which we believe have limitations. We are directing a significant portion of our efforts to address many of the limitations of eye drops while still delivering the drugs to the ocular surface. Our technology platform enables sustained drug delivery to the eye, which we believe can lead to increased compliance, enhanced efficacy and reduced side effects for our product candidates as compared to existing therapies. We are designing one of our sustained delivery product candidates so that following a single administration of one of our drug-eluting intracanalicular inserts for an acute condition or administration every several months for chronic conditions, a patient can receive continuous exposure to a therapeutic agent over a sustained period.

- *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.* We are focusing on completing the clinical development of our most advanced product candidates, including DEXTENZA for post-surgical ocular pain and inflammation and OTX-TP for glaucoma and ocular hypertension. We believe that the well-defined clinical and regulatory approval pathways for these product candidates, coupled with the availability of large patient populations, will enable us to complete clinical development in a capital and time efficient manner.

  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 of our manufacturing facility. We resubmitted our NDA 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. FDA concerns included deficiencies in manufacturing processes and analytical testing related to manufacturing of drug product identified during the pre-NDA approval inspection. We have corresponded with the FDA regarding these inspectional observations and are working to resolve the issues that have been identified. 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.

  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 in the fourth quarter of

2018. 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 will need to generate six-month (300 patients) and one year (100 patients) safety data during either the first or second Phase 3 clinical trial to support our product registration. At the same time, we are also advancing OTX-TIC, our travoprost-based intracameral implant for the treatment of moderate to severe glaucoma and ocular hypertension. We initiated a Phase 1 clinical trial outside the United States in the third quarter of 2017 and have submitted an IND during the first quarter of 2018 in the United States. We expect to initiate a second Phase 1 trial in the first half of 2018.

- *Apply our sustained-release intracanalicular insert technology for the treatment of additional diseases and conditions of the front of the eye*. We are exploring the potential use of our intracanalicular inserts in other front-of-the-eye diseases and conditions, such as dry eye disease and ocular infections, incorporating active pharmaceutical ingredients that are approved by the FDA as topical ophthalmic eye drops. We have completed an exploratory Phase 2 clinical trial of DEXTENZA for dry eye disease and a Phase 1 clinical trial of OTX-MP, an intracanalicular insert candidate, which incorporates the antibiotic moxifloxacin, to evaluate the safety and pharmacokinetics in OTX-MP in patients following cataract surgery. We may also pursue the development of a drug-eluting intracanalicular insert that delivers cyclosporine for the treatment of dry eye disease following a potential induction therapy using DEXTENZA. In addition, we may explore whether FDA-approved therapeutic agents that are not well suited to delivery by eye drops can be delivered by our intracanalicular inserts.

- *Pursue development of our intravitreal implant and other technologies for back-of-the-eye diseases and conditions*. We are developing a hydrogel-based 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 sustained release of the anti-angiogenic drugs over a four to six 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-based implant could potentially provide a more consistent level of therapeutic agent compared with existing therapies.

  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. We are also exploring the delivery of small molecule drugs, such as TKIs, in our hydrogel. We are conducting preclinical research on a TKI candidate that we selected for advancement to a potential first-in-humans clinical trial expected in the first half of 2018. We are also evaluating in early exploratory research additional opportunities beyond anti-VEGF drugs to utilize our hydrogel platform for back-of-the-eye diseases.

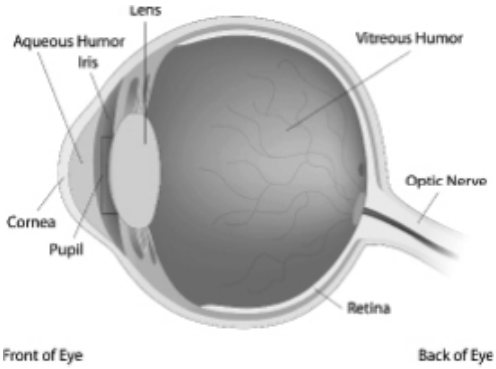
- *Maximize commercial potential of all products for which we receive marketing approval*. We hold worldwide commercial rights to each of our product candidates. We plan to prioritize our development, regulatory and commercialization efforts in the United States. We generally expect to retain commercial rights in the United States to any of our extended-delivery drug delivery product candidates for front-of-the-eye diseases and conditions for which we receive marketing approval. We may also consider co-promotion and other partnering arrangements in the United States as well. Outside 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 products of ours that receive marketing approval.

Eye Disease

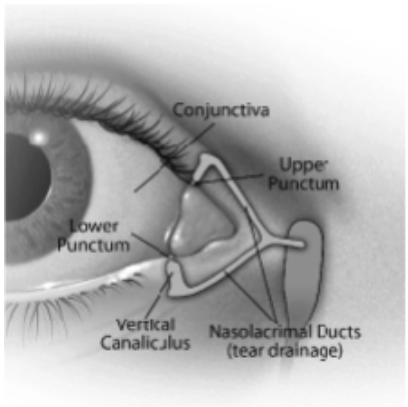
The front of the human eye consists of the cornea on the surface of the eye, the lens and the aqueous humor, which is a transparent fluid that fills the anterior chamber between the lens and the cornea. The tissue surrounding the eye also serves important functions. There is a natural opening, called 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.

Cross Section of Eye



Tear Drainage System



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 5.6 million ocular surgeries were to be performed in the United States in 2017.

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 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 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 22.0 million prescriptions were filled in the United States in 2017 for anti-inflammatory drugs administered by eye drops for ocular diseases and conditions, resulting in sales of approximately $3.8 billion. These prescriptions consisted of approximately 9.3 million prescriptions and $755 million in sales for single-agent corticosteroids, 3.6 million prescriptions and $351 million in sales for NSAIDs, 4.9 million prescriptions and $270 million in sales for corticosteroid and antibiotic combination products and approximately 4.3 million prescriptions and $2.4 billion in sales of Restasis and Xiidra for dry eye disease. According to IMS Health data, approximately 7.6 million anti-allergy eye drop prescriptions were filled in the United States in 2017, resulting in sales of approximately $667 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 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 36.1 million prescriptions were filled in the United States in 2017 for drugs administered by eye drops for the treatment of glaucoma, resulting in sales of approximately $2.8 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 2017. 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.

Ophthalmic bacterial infections are treated with a range of antibiotics, both branded and generic. One such example is moxifloxacin, a fourth generation fluoroquinolone marketed by Alcon under the brand names Vigamox and Moxeza. Fourth generation fluoroquinolones are favored because they offer the highest potency against gram-positive organisms while maintaining the gram-negative efficacy of previous generation antibiotics. In addition, the increased lipophilicity, or solubility in fatty tissue, of moxifloxacin allows for improved performance in ophthalmic tissue penetration studies compared to other fluoroquinolones. The relevant patents covering moxifloxacin expired in March 2014.

Market Data

According to IMS Health data, approximately 18.4 million prescriptions were filled in the United States in 2017 for ophthalmic antibiotics administered by eye drops, resulting in sales of approximately $560 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 2016, sales of Lucentis and Eylea totaled approximately $4.7 billion in the United States and $8.4 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 2017 there were to be approximately 4.0 million cataract extractions performed in the United States.

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

Sutures are the most widely used alternative method of wound closure. However, sutures do not completely prevent fluid leakage, are time-consuming to place and have been associated with patient discomfort, corneal distortion, and shallowing of the interior chamber. 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.

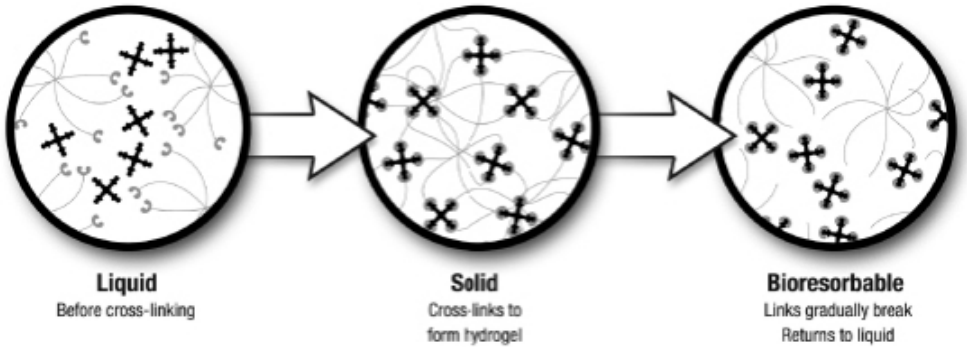
The Ocular Therapeutix Approach

Our Hydrogel Technology Platform

We apply our expertise with an established bioresorbable hydrogel technology to the development of products for sustained delivery of known, FDA-approved therapeutic agents for a variety of ophthalmic diseases and conditions and to ophthalmic wound closure. Our founders and management team 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 sustained 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.

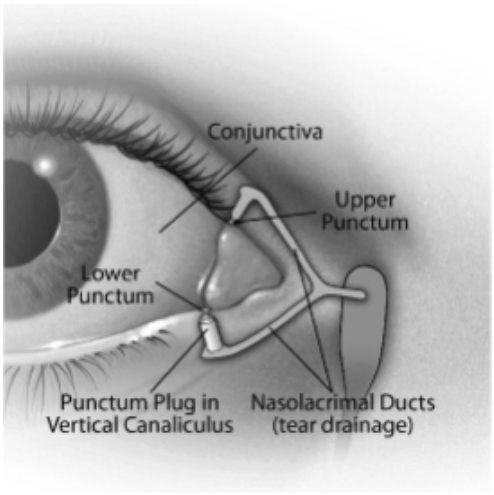


Intracanalicular Insert-Based Sustained-Release Therapies for Front-of-the-Eye Diseases and Conditions

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 sustained delivery of drug to the eye.

Intracanalicular insert shown positioned in the vertical canaliculus

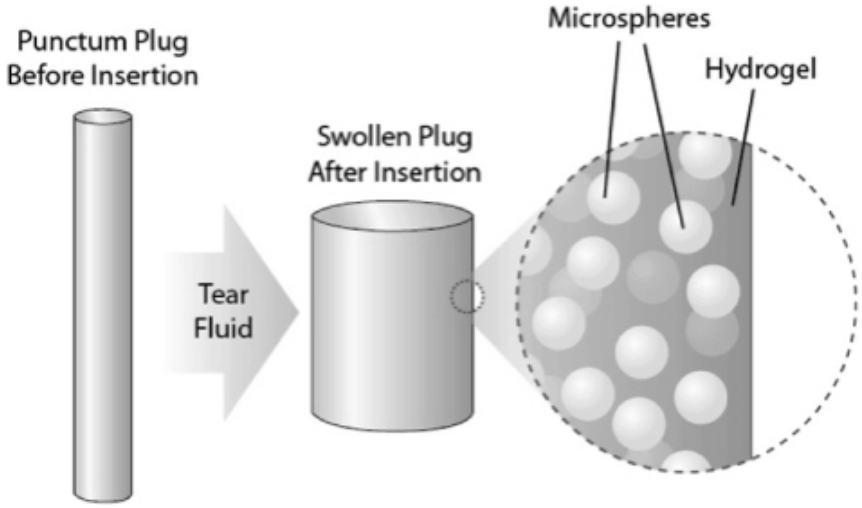


Our intracanalicular inserts utilize our proprietary hydrogel technology and are embedded with an active drug. Following insertion through the punctum, our inserts swell in tear fluid to fill the vertical canaliculus, which secures the inserts in place. We design our inserts to release drug in a sustained 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.

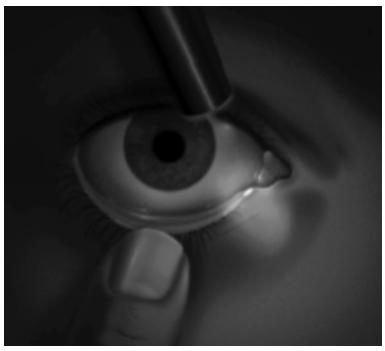
Our inserts allow incorporation of a variety of drugs with a controllable range of delivery durations and delivery rates. For acute conditions, such as post-surgical ocular pain and inflammation and allergic conjunctivitis, we have designed our intracanalicular inserts to provide a sustained release 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 sustained 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 sustained-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 sustained 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.
- *Sustained delivery of drug*. We have designed our intracanalicular inserts to deliver drug in a sustained 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 sustained 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 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

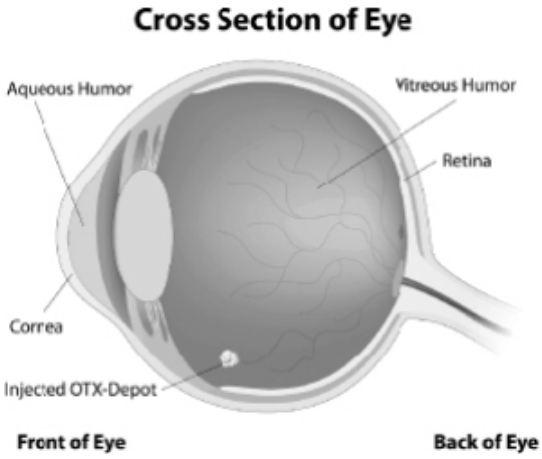
on the use of our extended-delivery hydrogel in combination with anti-angiogenic drugs such as protein-based anti-VEGF drugs or small molecule drugs, such as TKIs for the treatment of retinal diseases, such as wet AMD, retinal vein occlusion and diabetic macular edema. Our initial goal for these programs is to provide extended delivery 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 plan to initiate a human clinical trial outside of the United States in the first half of 2018. We have conducted preclinical work on this compound and have achieved sustained delivery 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.

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 sustained 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 2018.

Development Pipeline and Marketed Product

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

Product / Program	Indication	Description (Active Pharmaceutical Ingredient)	Stage of Development	Status
Approved Product				
ReSure Sealant	Cataract incision closure	Ocular sealant	Marketed	Approved by the FDA in January 2014; commercially launched in the United States in February 2014
Late Stage Product Candidates				
DEXTENZA	Post-surgical ocular pain and inflammation	Intracanalicular insert (Dexamethasone)	Phase 3	Two Phase 3 trials completed in the first quarter of 2015; third Phase 3 trial topline results reported for treatment of post-surgical ocular inflammation in November 2016; NDA resubmission for ocular pain anticipated in the first half of 2018
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
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

Product / Program	Indication	Description (Active Pharmaceutical Ingredient)	Stage of Development	Status
Approved Product				
Earlier Stage Product Candidates				
DEXTENZA	Dry eye disease	Intracanalicular insert (Dexamethasone)	Phase 2	Topline results from Phase 2 trial reported in December 2015
OTX-MP	Ocular infection	Intracanalicular insert (Moxifloxacin)	Phase 1 completed	No active development efforts
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 and plan to initiate a second Phase 1 clinical trial in the first half of 2018 in the U.S.
Anti-angiogenic hydrogel implants				
Sustained-release Aflibercept	Wet AMD	Intravitreal implant (Protein-based anti-angiogenic compound)	Preclinical	Ongoing preclinical studies
OTX-TKI	Wet AMD	Intravitreal implant (Tyrosine kinase inhibitor anti-angiogenic compound)	Preclinical	Plan to initiate a Phase 1 clinical trial outside of the U.S. in the first half of 2018

Dexamethasone Intracanalicular Insert

Our DEXTENZA (sustained-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, allergic conjunctivitis and dry eye disease. 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 sustained 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 sustained delivery of drug to the eye may result in better control of ocular pain and inflammation as compared to 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, allergic conjunctivitis, and dry eye disease. 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, which states the FDA has determined that it cannot approve the NDA in its present form. FDA concerns included deficiencies in manufacturing processes and analytical testing related to manufacturing of drug product identified during the pre-NDA approval inspection. We have corresponded with the FDA regarding these inspectional observations and are working to resolve the issues that have been identified. 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 have undertaken in response to the FDA's inspectional observations and as a result of further internal review include upgrades to our manufacturing equipment and updates to our manufacturing processes and quality oversight. These changes are 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. In December 2017, we requested a meeting with the FDA to describe our remediation efforts and NDA resubmission plans and to seek feedback. A meeting was granted in January 2018, and we believe that the preliminary written responses from the FDA to our questions fully addressed our meeting objectives. We decided that the meeting would no longer be necessary because of the completeness of the FDA's response and that the FDA's comments do not require any substantial change in our manufacturing or regulatory plans. As a result, the correspondence with the FDA will represent the official record of that previously scheduled meeting. As a result the correspondence with the FDA will represent the official record of that previously scheduled meeting. Subject to satisfactorily addressing the FDA inspectional observations and demonstrating consistency in our commercial stage manufacturing process, we plan to resubmit our NDA for DEXTENZA for the treatment of post-surgical ocular pain in the first half of 2018. Adequate resolution of the outstanding Form 483 inspectional observations and the final decision as to the adequacy of our manufacturing processes are determined by the FDA with input from the Office of Process and Facilities within CDER, as part of the NDA review process, and are necessary prior to NDA approval.

- 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 assessing our plans for our dry eye program going forward.

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.

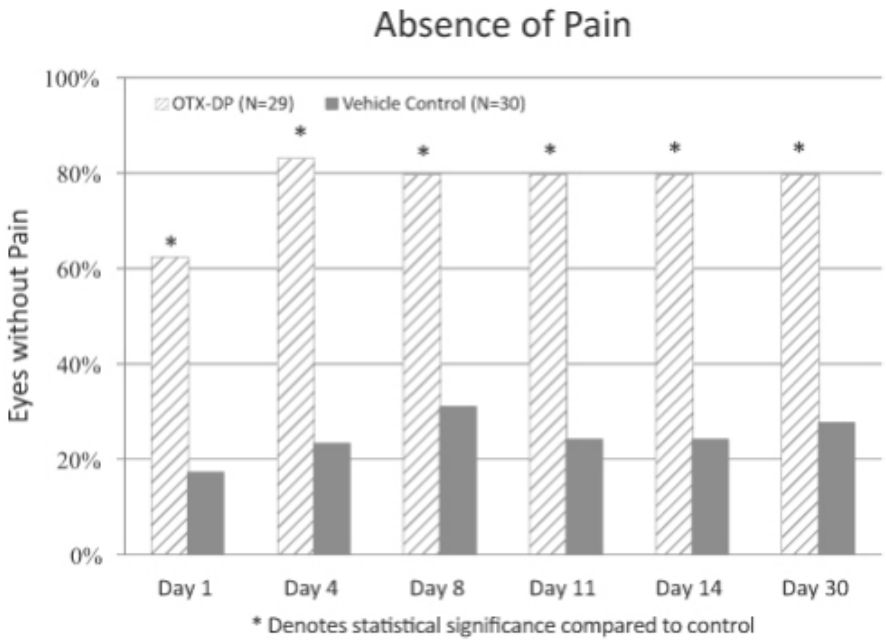
One of our goals for this trial was to determine the appropriate primary endpoints for a subsequent Phase 3 clinical development program. The two primary efficacy measures in this trial were absence of inflammatory cells in the anterior chamber of the study eye and absence of pain in the study eye. When 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.

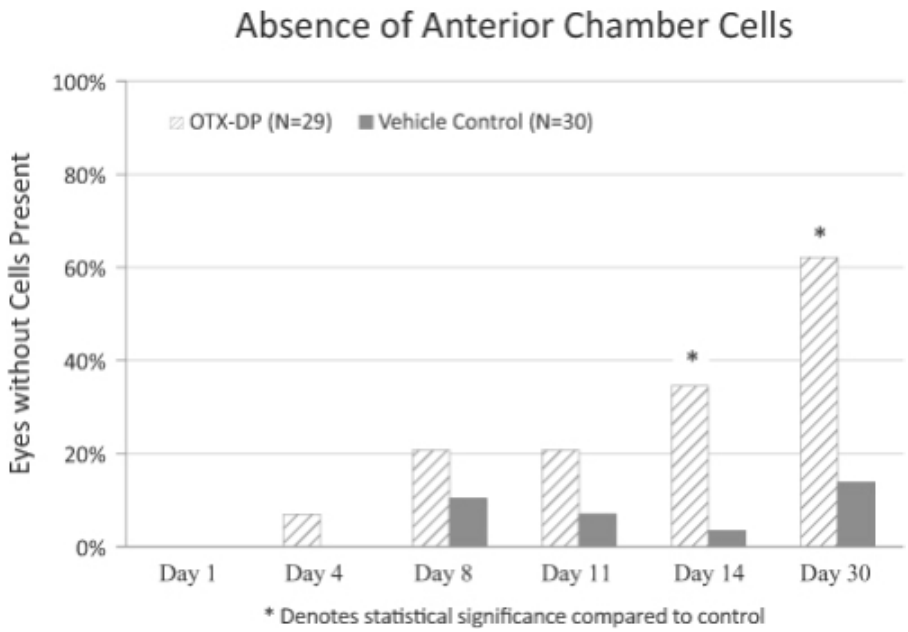
We enrolled patients in this trial who were at least 21 years of age undergoing unilateral clear corneal cataract surgery. We excluded patients from the trial if, among other reasons, they had intraocular inflammation or ocular pain in the study eye at screening or had glaucoma or ocular hypertension.

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.

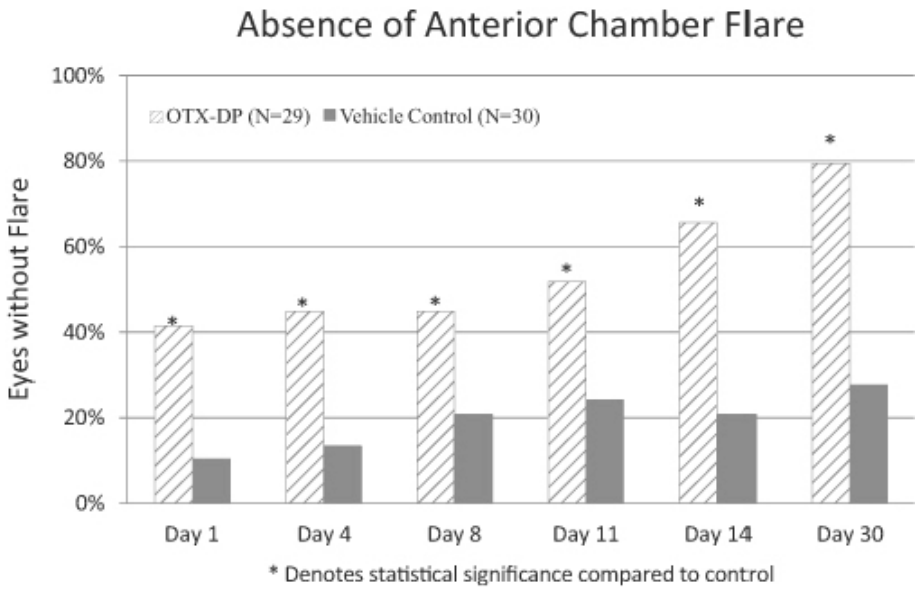


In this trial, DEXTENZA did not meet the primary efficacy endpoint with statistical significance for absence of cells in the anterior chamber compared to the vehicle control at day 8. However, there was a trend of improved absence

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.

Subject to satisfactorily addressing the FDA inspectional observations and demonstrating consistency in our commercial stage manufacturing process, we plan to resubmit our NDA for DEXTENZA for the treatment of post-surgical ocular pain in the first half of 2018. Adequate resolution of the outstanding Form 483 inspectional observations and the final decision as to the adequacy of our manufacturing processes are determined by the FDA with input from the Office of Process and Facilities within CDER as part of the NDA review process and are necessary prior to NDA approval. Subject to receiving approval for the pain indication pursuant to the NDA resubmission, we plan to submit an 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. We expect that we would submit the sNDA under Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, or FDCA. See "—Government Regulation—Section 505(b)(2) NDAs" for additional information. 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:

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

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

Phase 3 Clinical Program

We met with the FDA in December 2014 to review the Phase 2 clinical trial results of DEXTENZA for the treatment of allergic conjunctivitis and to discuss our planned Phase 3 clinical development program. Based on these discussions, we have 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	DEXTENZA	Vehicle	Treatment Difference (P-value)
Ocular Itching	3 min	1.68 (1.032)	2.66 (0.861)	**-1.02 (<0.0001)**
	5 min	1.87 (1.04)	2.74 (0.69)	**-0.87 (<0.0001)**
	7 min	1.70 (0.938)	2.74 (0.679)	**-1.04 (0.0007)**
Conjunctival Redness	7 min	1.52 (0.641)	1.80 (0.764)	**-0.26 (0.1082)**
	15 min	1.48 (0.698)	1.75 (0.786)	**-0.32 (0.0419)**
	20 min	1.44 (0.710)	1.76 (0.766)	**-0.29 (0.0667)**

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

Second Phase 3 Clinical Trial

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

Safety: There were no serious adverse events reported in this trial. There were a variety of adverse events in both the DEXTENZA group and the vehicle control group, with six patients in the DEXTENZA treatment group with a total of six ocular and one non-ocular adverse events and 11 patients in the vehicle control group with a total of nine ocular and eight non-ocular adverse events. The lower rate of ocular adverse events in the DEXTENZA group could potentially be due to the presence of an anti-inflammatory active pharmaceutical ingredient. Ocular adverse events reported more than one patient in either treatment group included increased IOP, which was experienced by two patients in the DEXTENZA group, as well as dacryostenosis acquired and dacryocanaliculitis, each experienced by two patients in the vehicle control group. Both cases of IOP increased were considered treatment related, as were both cases of dacrycanaliculitis 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. Based on the results from the second Phase 3 clinical trial in which we failed to meet the primary efficacy endpoints, we may conduct a third Phase 3 clinical trial. Subject to receiving approval for DEXTENZA for the treatment of post-surgical ocular pain pursuant to the NDA that has been submitted to the FDA and obtaining favorable results from any such 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.

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 expect to enroll approximately 550 patients at 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 sustained delivery 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:

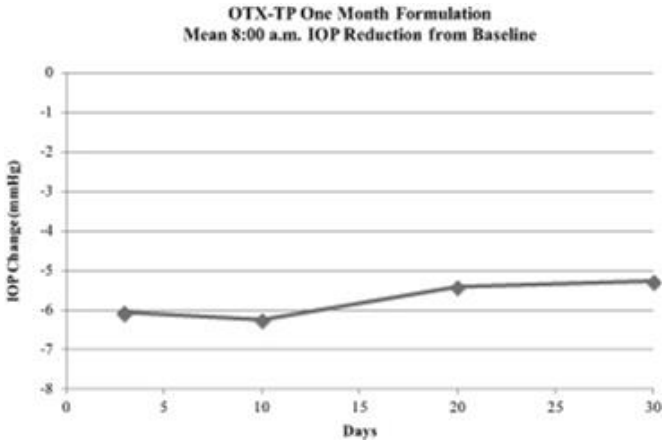
- mean IOP at 8:00 a.m. at each evaluation date as measured in millimeters of mercury, or mmHg;
- mean IOP at 10:00 a.m. and 4:00 p.m. at days 10, 20 and 30;
- change in mean IOP from baseline at each time point measured; and
- retention of the insert in the canaliculus at days 10, 20 and 30.

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

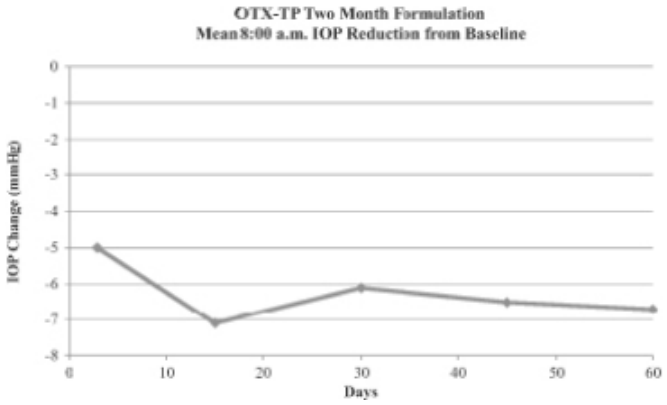
In 2012, we completed a prospective, single arm, open label pilot study evaluating the initial safety and efficacy of the two-month version of OTX-TP for the treatment of glaucoma and ocular hypertension. We conducted this trial in 20 patients, and in 36 eyes, at two sites in South Africa.

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.

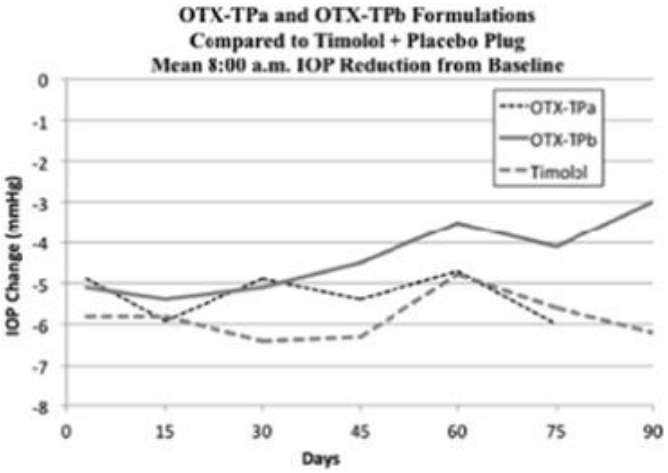
We evaluated safety in all patients at each study visit with an assessment of general eye conditions, including visual acuity, along with any adverse events.

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:

8:00 am Results for IOP (mmHg)

	Intent to Treat Population		**Post-hoc analysis Baseline of 5 weeks, single drug only**	
	OTX-TP	**Timolol**	**OTX-TP**	**Timolol**
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
Average	-4.8	-7.0	-5.6	-6.7
Difference	**-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 expect to enroll 550 patients at up to 50 sites in our first Phase 3 clinical trial for an 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. We do not intend to initiate the second Phase 3 clinical trial until we receive data from the first Phase 3 clinical trial and may determine to discuss the results of this first Phase 3 clinical trial with the FDA prior to initiating a second Phase 3 clinical trial.

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

We are conducting preclinical development of OTX-TIC, our product candidate, 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 have not enrolled any patients in this clinical trial as of February 28, 2018. The study is expected to be a prospective, single-center study to evaluate the safety, efficacy, durability and tolerability of OTX-TIC compared to topical travoprost (eye drops) in up to 20 patients with open-angle glaucoma or ocular hypertension. We submitted an IND in the first quarter of 2018 and expect to initiate a second Phase 1 trial in the United States in the first half of 2018.

Moxifloxacin Intracanalicular Insert (OTX-MP)

Our OTX-MP product candidate incorporates the antibiotic moxifloxacin as an active pharmaceutical ingredient. We have completed a Phase 1 clinical trial of OTX-MP evaluating safety and pharmacokinetics in patients following cataract surgery. Although we believe that OTX-MP has potential to treat bacterial conjunctivitis and corneal ulcers, we are currently prioritizing our allocation of resources to the clinical development of our DEXTENZA and OTX-TP clinical development programs and do not have plans currently to allocate clinical development resources to later stage clinical testing of OTX-MP. We will continue to assess our strategy and, if resources are available to fund this program, we would expect to initiate additional clinical trials to evaluate OTX-MP for a particular ocular infection indication. If we determine to proceed with later stage clinical testing of OTX-MP, we expect to select the specific indication for clinical development based on our assessment of clinical and regulatory pathways, including the relative expected costs and availability of our resources.

We selected moxifloxacin as the active pharmaceutical ingredient for OTX-MP because it:

- is approved by the FDA for bacterial conjunctivitis;
- is available on a generic basis;
- offers high lethality against gram-positive organisms while maintaining gram-negative lethality;
- is available from multiple qualified suppliers; and
- has physical properties that are well suited for incorporation within our intracanalicular inserts.

Completed Phase 1 Clinical Trial

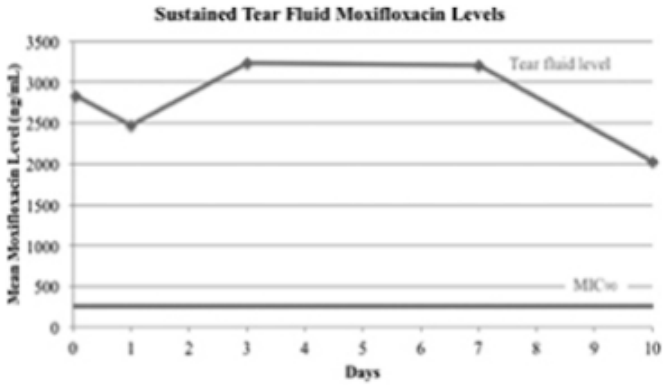
In 2010, we completed a prospective, single center, single arm, open label Phase 1 clinical trial evaluating the initial safety and pharmacokinetics of OTX-MP in post-cataract surgery patients. We conducted the trial in 10 patients at one site in Singapore.

We enrolled patients in this trial who were at least 21 years of age undergoing clear corneal cataract surgery. We evaluated patients at days 1, 3, 7, 10, 20 and 30 following insertion of the insert and made the following assessments:

- retention of the insert in the canaliculus on each evaluation date;
- moxifloxacin level in tear fluid on each evaluation date; and
- ease of use.

Efficacy: We have designed our OTX-MP product candidate to provide for the release of moxifloxacin over a period of up to two weeks and to be fully resorbed by day 30. In this trial, the insert was present in 100% of eyes through day 10 and 0% of eyes at day 30. This indicates the insert functioned as designed for retention and for resorption. The mean concentration level of moxifloxacin in tear fluid at each post-surgical evaluation date through day 10 was above the MIC_{90} potency threshold. The MIC_{90} measurement establishes the concentration of a drug needed to inhibit the growth of 90% of a panel of bacterial strains isolated from patients. OTX-MP was able to maintain effective

concentration levels of moxifloxacin in the tear fluid over the target 7 to 10 day period, as shown in the chart below. No drug was detectable at day 30.



The investigator who administered the OTX-MP rated the product as “easy” to use for nine of 10 (90%) cases and as “difficult” to use in one (10%) of the cases.

Safety: There were no serious adverse ocular events or other significant adverse ocular events in this trial.

Regulatory Pathway

If we were to advance the clinical development of our OTX-MP product candidate for the treatment of a particular ocular infection indication, we would expect to initiate a Phase 2 clinical trial to evaluate OTX-MP for such indication. We would then be required to successfully complete two well controlled Phase 3 clinical trials conducted under an IND to obtain marketing approval from the FDA. At least one of the Phase 3 clinical trials would be conducted in the United States. If we were to obtain favorable results from these two pivotal clinical trials, we would plan to submit an NDA to the FDA for marketing approval of OTX-MP for such indication. We expect that we would submit this NDA under Section 505(b)(2) of the FDCA. See “—Government Regulation—Section 505(b)(2) NDAs.”

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 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 are also researching the delivery of small molecule TKIs from our hydrogel and have selected the TKI we plan to advance to an initial human clinical trial outside the United States in the first half of 2018. We have conducted preclinical work on this compound and have achieved sustained delivery 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 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 sustained delivery 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 sustained 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 are currently conducting studies with Regeneron to demonstrate sustained delivery and tolerability of aflibercept. 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. Additional dose ranging and tolerability studies are currently in progress.

We plan to continue working with our collaboration partner Regeneron on our protein-based anti-VEGF program for the treatment of back-of-the-eye diseases. 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.

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 sales support provided to the product at this time, but if DEXTENZA is approved for marketing, we expect to be able to sell ReSure Sealant with DEXTENZA with any sales force we establish for DEXTENZA. ReSure Sealant is not separately reimbursed when used as part of a cataract surgery procedure.

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

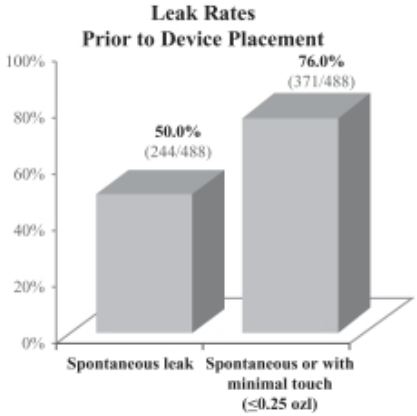
In 2013, we completed a prospective, randomized, parallel-arm, controlled, multicenter, subject-masked pivotal clinical trial evaluating the safety and effectiveness of ReSure Sealant. In this trial, we enrolled 488 patients at 24 sites across the United States. One patient was excluded prior to treatment 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-

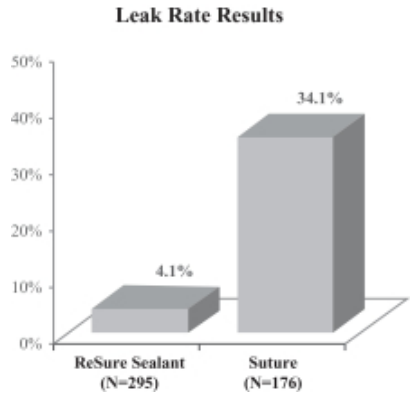
inferiority margin for the ReSure Sealant pivotal clinical trial was a percentage difference in leak rates between ReSure Sealant and sutures of 5%.

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, 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. Enrollment into this study has not been met to date, and discussions are ongoing with the FDA to develop a path forward to complete this post-approval study requirement. Any concerns raised by the FDA due to its review of the results from these post-approval studies or our failure to complete the Device Exposure Registry could lead to modification in product labeling or the approved indication for use or could generate negative publicity which would impact our commercialization efforts.

Foreign Approvals

Outside the United States, we plan to assess whether to seek regulatory approval for ReSure Sealant in markets such as the European Union, Australia and Japan based on the market opportunity, particularly pricing, and the requirements for marketing approval. Given our prioritization of the clinical development of our sustained-release product candidates and our planned commercialization efforts for our initial intracanalicular insert product candidates in the United States, we do not currently plan to seek CE Mark approval to commercialize ReSure Sealant in the European Union. Outside of the United States and the European Union, we will need to engage a third party to assist us in the approval process. If we obtain regulatory approval to market and sell ReSure Sealant in international markets, we expect to utilize a variety of types of collaboration, distribution and other marketing arrangements with one or more third parties to commercialize ReSure Sealant. See “—Government Regulation—Review and Approval of Medical Devices in the European Union” for additional information.

Sales, Marketing and Distribution

We 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, if DEXTENZA is approved for marketing, 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 sustained-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. Subject to satisfactorily addressing the FDA inspectional observations, we plan to resubmit our NDA for DEXTENZA for the treatment of post-surgical ocular pain in the first half of 2018. Subject to receiving FDA approval for the pain indication pursuant to the NDA, we plan to submit an sNDA for DEXTENZA for the treatment of post-surgical ocular inflammation, in order to get label expansion for this indication. If DEXTENZA is approved for marketing, we are considering potential commercialization options for DEXTENZA in the United States, including building our highly targeted, key account sales force that would focus on the ambulatory surgical centers responsible for the largest volumes of cataract surgery. If OTX-TP is approved for marketing, we may use a combination of a contract sales organization, or CSO, and direct sales representatives, and potentially expand the size of the team, to commercialize OTX-TP as well. 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. We are also developing a TKI product candidate for the treatment of retinal diseases including wet AMD, which is also at a preclinical stage of development. We plan to initiate a Phase 1 clinical trial outside the United States in the first half of 2018 to assess the safety, durability, and tolerability of OTX-TKI in the posterior segment of the human eye for the treatment of VEGF induced retinal leakage for an extended duration. If we receive FDA approval of this product candidate, we may elect to commercialize this product through a direct sales force or enter into a strategic collaboration with a partner and license the commercial rights.

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.

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 field of human ophthalmic diseases and conditions. As of March 1, 2018, we have licensed from Incept a total of 21 U.S. patents, 9 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 seven 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. Three U.S. patents which are expected to expire between 2018 and 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 that will expire in 2018 and 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 OTX-DP 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 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.

Financial Terms. In connection with the agreement, we issued to Incept 443,068 shares of our common stock. In addition, on February 12, 2014, we issued to Incept 189,393 shares of our common stock in connection with the expansion of the scope of the license to include back-of-the-eye technology held by Incept. We are obligated to pay Incept a royalty equal to a low single-digit percentage of net sales made by us or our affiliates. 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.

Assignment of Our Patents. Under the terms of the agreement, we have agreed to assign to Incept our rights in any patent application 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.

Patent Prosecution and Litigation. The agreement provides that, with limited exceptions, Incept has sole control and responsibility for ongoing prosecution for the patents covered by the license agreement. We have the right to bring suit against third parties who infringe the patents covered by the license agreement, but we have 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 license agreement. We are responsible for all costs incurred in prosecuting any infringement action we bring.

Term and Termination. The agreement, unless earlier terminated by us or Incept, will remain in effect until the expiration of the last to expire patent or patent application licensed to us under the agreement. The agreement provides that either party may terminate the 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 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-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.

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 its 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.

Competitors of OTX-TP

Allergan, Inc. is conducting Phase 3 clinical development of 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. Envisia Therapeutics is in Phase 2 clinical development of a sustained delivery product candidate delivering travoprost 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. Alcon is developing the Replenish pump to deliver its anti-VEGF agent.

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, 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

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. To date, we have submitted two INDs to the FDA. The first IND was submitted in August 2012 and relates to DEXTENZA for the treatment of post-surgical ocular pain and inflammation and, pursuant to subsequent amendments submitted in February and November 2014, allergic conjunctivitis and dry eye disease. We submitted a second IND to the FDA relating to OTX-TP for the treatment of glaucoma and ocular hypertension in the second half of 2014 prior to initiating our Phase 2b clinical trial of OTX-TP for this indication.

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

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.

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 2018 is $2,421,495 for an application requiring clinical data. The sponsor of an approved application is also subject to an annual program fee, which for fiscal year 2018 is $304,162. 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.

The FDA's Decision on an NDA or BLA

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.

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 a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug."

Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. 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, 2018, the FDA has approved nine 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.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application. With regard to patents, the six-month pediatric exclusivity period will not attach to any patents for which an ANDA or 505(b)(2) applicant submitted a paragraph IV patent certification, unless the NDA sponsor or patent owner first obtains a court determination that the patent is valid and infringed by the proposed product.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate

approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The United States Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Review and Approval of Medical Devices in the United States

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

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

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

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

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

510(k) Premarket Notification

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

has the same intended use as a predicate device and the same technological characteristics, or the same intended use and different technological characteristics and does not raise new questions of safety and effectiveness than the predicate device.

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

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

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

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

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

Premarket Approval Application

The PMA application process for approval to market a medical device is more complex, costly, and time- consuming than the 510(k) clearance procedure. A PMA application must be supported by extensive data, including technical information regarding device design and development, preclinical studies, clinical trials, manufacturing and controls information and labeling information that demonstrate the safety and effectiveness of the device for its intended use. After a PMA application is submitted, the FDA has 45 days to determine whether it is sufficiently complete to permit a substantive review. If the PMA application is complete, the FDA will file the PMA application. If the FDA accepts the application for filing, the agency will begin an in-depth substantive review of the application. By statute, the FDA has 180 days to review the application although, generally, review of the application often takes between one and three years, and may take significantly longer. If the FDA has questions, it will likely issue a first major deficiency letter within 150 days of filing. It may also refer the PMA application to an FDA advisory panel for additional review, and will conduct a preapproval inspection of the manufacturing facility to ensure compliance with the QSR, either of which could extend the 180-day response target. In addition, the FDA may request additional information or request the performance of additional clinical trials in which case the PMA application approval may be delayed while the trials are conducted

and the data acquired are submitted in an amendment to the PMA. Even with additional trials, the FDA may not approve the PMA application.

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

PMA applications are subject to an application fee. For federal fiscal year 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.

The 21st Century Cures Act

On December 13, 2016, President Obama signed the 21st Century Cures Act, or Cures Act, into law. The Cures Act is designed to modernize and personalize healthcare, spur innovation and research, and streamline the discovery and development of new therapies through increased federal funding of particular programs. It authorizes increased funding for the FDA to spend on innovation projects. The new law also amends the Public Health Service Act to reauthorize and expand funding for the NIH. The Cures Act establishes the NIH Innovation Fund to pay for the cost of development and implementation of a strategic plan, early stage investigators and research. It also charges NIH with leading and coordinating expanded pediatric research. Further, the Cures Act directs the Centers for Disease Control and Prevention to expand surveillance of neurological diseases.

With amendments to the FDCA and the Public Health Service Act, or PHSA, Title III of the Cures Act seeks to accelerate the discovery, development, and delivery of new medicines and medical technologies. To that end, and among other provisions, the Cures Act reauthorizes the existing priority review voucher program for certain drugs intended to treat rare pediatric diseases until 2020; creates a new priority review voucher program for drug applications determined to be material national security threat medical countermeasure applications; revises the FDCA to streamline review of combination product applications; requires FDA to evaluate the potential use of "real world evidence" to help support approval of new indications for approved drugs; provides a new "limited population" approval pathway for antibiotic and antifungal drugs intended to treat serious or life-threatening infections; and authorizes FDA to designate a drug as a "regenerative advanced therapy," thereby making it eligible for certain expedited review and approval designations.

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 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 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).

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

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

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

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

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 expect to apply for a transitional pass-through reimbursement code, or C code, from the CMS for DEXTENZA for the treatment of post-surgical ocular pain, subject to the approval of the NDA we filed with the FDA for this indication. 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 have submitted an application to the CMS for a J code for DEXTENZA 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 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 been 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.

Further, 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 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. 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. 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. In January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In October 2017, President Trump signed a second Executive Order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the ACA exchanges. At the same time, the Trump Administration announced that it will discontinue the payment of cost-sharing reduction, or CSR, payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain.

There have been, and likely will continue to be, additional legislative and regulatory proposals at the foreign, federal, and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. Such reforms could have an adverse effect on anticipated revenues 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 product candidates.

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. 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. 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.

Employees

As of March 1, 2018, we had 119 full-time employees. Of these full-time employees, 97 employees are primarily engaged in research and development activities. In 2017, 2016, and 2015, we spent $30.9 million, $27.1 million, and $26.6 million, respectively, on company-sponsored 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.

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. You can find, copy and inspect information we file at the SEC's public reference room, which is located at 100 F Street, N.E., Room 1580, Washington, DC 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the SEC's public reference room. You can review our electronically filed reports and other information that we file with the SEC on the SEC's web site at http://www.sec.gov. 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 $39.7 million for the year ended December 31, 2015, $44.7 million for the year ended December 31, 2016 and $63.4 million for the year ended December 31, 2017. As of December 31, 2017, we had an accumulated deficit of $237.3 million. Through December 31, 2017, 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 in preparation for a potential commercial launch of DEXTENZA. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year.

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

- continue to pursue the clinical development of our most advanced intracanalicular insert product candidates, DEXTENZA and OTX-TP;
- commence 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-based

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;
- seek marketing approvals for any of our product candidates that successfully complete clinical development;
- develop and expand our sales, marketing and distribution capabilities for any of our product candidates, including DEXTENZA, for which we may obtain marketing approval;
- 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;
- 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 is currently 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. Instead, for us to become and remain profitable, we will need to succeed in developing and commercializing products with greater market potential. This will require us or our current or future collaborators to be successful in a range of challenging activities, including:

- successfully completing clinical development of our product candidates;
- obtaining marketing approval for these product candidates;
- manufacturing at commercial scale, marketing, selling and distributing 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.

We may never succeed in these activities and may never generate revenue that is sufficient or great enough to achieve profitability. In July 2016, we received a Complete Response Letter, or CRL, from the FDA regarding our new drug application, or NDA, for DEXTENZA for the treatment of post-surgical ocular pain. This 2016 CRL pertained to deficiencies in manufacturing process and controls identified during a pre-NDA approval inspection of our manufacturing facility performed by the FDA New England District Office, or the District Office, in February 2016 that were documented on FDA Form 483. In November 2016, we received notice from the District Office accepting that our responses satisfactorily addressed the remaining corrective actions in the Form 483. Since receiving the CRL, we have also had ongoing communications with the FDA, including the New England District Office and offices within the Center for Drug Evaluation and Research, or CDER, including the Office of Process and Facilities, with regard to the manufacturing issues and our plan for a resubmission of our NDA. 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 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. FDA concerns included deficiencies in manufacturing processes and analytical testing related to manufacturing of drug product identified during the pre-NDA approval inspection. We have corresponded with the FDA regarding these inspectional observations and are working to resolve the issues that have been identified. 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 have undertaken in response to the FDA's inspectional observations and as a result of further internal review include upgrades to our manufacturing equipment and updates to our manufacturing processes and quality oversight. These changes are 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. In December 2017, we requested a meeting with the FDA to describe our remediation efforts and NDA resubmission plans and to seek feedback. A meeting was granted in January 2018, and we believe that the preliminary written responses from the FDA to our questions fully addressed our meeting objectives. We decided that the meeting would no longer be necessary because of the completeness of the FDA's response and that the FDA's comments do not require any substantial change in our manufacturing or regulatory plans. As a result, the correspondence with the FDA will represent the official record of that previously scheduled meeting. Subject to satisfactorily addressing the FDA inspectional observations and demonstrating consistency in our commercial stage manufacturing process, we plan to resubmit our NDA for DEXTENZA for the treatment of post-surgical ocular pain in the first half of 2018. Adequate resolution of the outstanding Form 483 inspectional observations and the final decision as to the adequacy of our manufacturing processes are determined by the FDA, with input from CDER's Office of Process and Facilities, as part of the NDA review process, and are necessary prior to NDA approval. If we are unable to resolve these inspectional observations in a timely manner or achieve consistency in our commercial stage manufacturing process, our resubmission of our NDA and its potential approval would be delayed or prevented.

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 conduct late stage clinical trials for our extended-delivery drug delivery product candidates, in particular DEXTENZA

and OTX-TP, and seek marketing approval for any such product candidate for which we obtain favorable pivotal clinical results. We also expect to devote significant financial resources to conducting research and development and potentially seeking regulatory approval for our other product candidates. In addition, we plan to devote substantial financial resources to our commercialization efforts, including product manufacturing, sales, marketing and distribution for any of our product candidates, including DEXTENZA, for which we may obtain marketing approval in the future. 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, 2017, we had cash and cash equivalents of $41.5 million and outstanding debt of $18.0 million. In January 2018, we completed a follow-on offering of our common stock at a public offering price of $5.00 per share, in which we received net proceeds of approximately $35.1 million after deducting underwriting discounts and commissions. Based on our current plans and forecasted expenses, we believe that our existing cash and cash equivalents, as of December 31, 2017, along with the proceeds from our public offering of common stock in January 2018 but 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 through the first quarter of 2019. 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. We have not reflected the full costs of building a sales force that we would build if DEXTENZA is approved for marketing in our current operating plan and will need to raise additional capital to support such an effort. Our future capital requirements will depend on many factors, including:

- the costs, timing and outcome of regulatory review of our product candidates by the FDA, the EMA or other regulatory authorities, including the resubmission of our NDA for DEXTENZA;
- the level of product sales from 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 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 DEXTENZA and OTX-TP;
- 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-based 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 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 outcome of certain 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 is a 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 financial statements included in this Annual Report on Form 10-K.

Our audited financial statements for the period ended December 31, 2017 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 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 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 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 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.

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 current credit facility, as amended, we had $18.0 million of outstanding principal amount of indebtedness as of December 31, 2017. Our obligations under this facility are secured by all of our assets other than our intellectual property. Our intellectual property rights are subject to a negative pledge arrangement under the facility. 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 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 could result in an event of default under those instruments. In the event of an acceleration of amounts due under our credit facility 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, the pledge of our assets as collateral and the negative pledge of our intellectual property 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 and, beginning in the first quarter of 2014, commercializing ReSure Sealant. 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 will need to transition 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 our intracanalicular insert and other product candidates, in particular DEXTENZA 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 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 pain and 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 these product candidates will receive marketing approval. Our ability to generate product revenues sufficient to achieve profitability will depend heavily on our obtaining marketing approval for and commercializing one or both of DEXTENZA and OTX-TP.

The commercial success of our intracanalicular insert and other 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 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 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 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.

According to the trial protocols, the two primary efficacy endpoints in our completed Phase 2 and the first two Phase 3 clinical trials are fixed sequence endpoints. As such, a statistical analysis of the trial results required that we first assess the primary endpoint regarding absence of inflammatory cells in the study eye. The protocol and statistical analysis plan for the trial did not contemplate assessing the primary endpoint regarding absence of pain in the study eye in the event the clinical trial of DEXTENZA did not meet the first primary endpoint with statistical significance. The FDA has informed us that the hierarchy of the two primary endpoints for post-surgical ocular pain and inflammation is applicable in connection with their review of our NDA seeking approval for DEXTENZA for an ocular pain indication. However, the FDA has also informed us that pain endpoints from the Phase 2 and first two Phase 3 trials, with respect to which we received favorable data, would support the NDA submission. Therefore, in September 2015, we submitted to the FDA an NDA for DEXTENZA for an ocular pain indication using the existing data from our completed Phase 2 and first two Phase 3 clinical trials notwithstanding the FDA's comment regarding the applicability of the hierarchy of the two primary endpoints in our completed Phase 2 and Phase 3 clinical trials. In July 2017, we received a CRL from the FDA regarding our resubmitted NDA for DEXTENZA stating that the FDA has determined that it cannot approve the NDA in its present form. FDA concerns included deficiencies in manufacturing process and analytical testing related to manufacturing of drug product identified during a pre-NDA approval inspection of our manufacturing facility. In our response to the FDA regarding these deficiencies, we also had to furnish a safety update regarding all completed trials of DEXTENZA, regardless of indication, dosage form or dose level.

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 to include inflammation. 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 subject to resubmitting and receiving approval for the pain indication pursuant to the initial NDA, we plan to submit an NDA supplement, or sNDA, for DEXTENZA for the treatment of post-surgical ocular inflammation. Although we believe our planned approach for seeking marketing approval of DEXTENZA is supported by our discussions with the FDA and by the absence of any efficacy or safety concerns identified by the FDA in the CRL with respect to the clinical data provided in the NDA, the FDA could nonetheless not grant marketing approval of DEXTENZA for the pain indication until we submit complete results from the third Phase 3 clinical trial, or at all.

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 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 the superiority of OTX-TP 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, will not include a timolol active comparator and will not have eye drops, placebo or active, administered in either the treatment or the placebo-controlled arm. 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 may determine to discuss the results of this first Phase 3 clinical trial with the FDA prior to initiating a second Phase 3 clinical trial. 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 continue to 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 extended-delivery 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 extended-delivery 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, but have not enrolled any patients in this trial as of February 28, 2018.

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 is expected to enroll approximately 550 patients at approximately 50 sites in the United States and will be the largest clinical trial we will have conducted to date. Patients randomized into the placebo control arm will not receive any glaucoma medications during the course of this trial. Our inability to enroll a sufficient number of patients in our first Phase 3 clinical trial or 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 of our extended-delivery drug delivery product candidates or any other product candidates that we may develop, we may need to abandon or limit our development of such product candidates.

If our extended-delivery drug delivery product candidates or any of our other product candidates are associated with serious adverse events or undesirable side effects in clinical trials or have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the serious adverse events, undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. In each of our first two Phase 3 clinical trials of DEXTENZA for the treatment of post-surgical ocular 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 dacryocanaliculitis, 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 product candidates based on our bioresorbable hydrogel technology platform other than 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 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 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-based drug delivery implants designed to release therapeutic antibodies and small molecules such as TKIs, to modulate the biologic 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-based 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 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 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 candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

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 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 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 in obtaining regulatory approvals of our product candidates and meeting customer demand for ReSure Sealant, 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 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 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. FDA concerns included deficiencies in manufacturing processes and analytical testing related to manufacturing of drug product identified during the pre-NDA approval inspection. We have corresponded with the FDA regarding these inspectional deficiencies and are working to resolve the issues that have been identified. We have corresponded with the FDA regarding these inspectional observations and are working to resolve the issues that have been identified. 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 have undertaken in response to the FDA's inspectional observations and as a result of further internal review include upgrades to our manufacturing equipment and updates to our manufacturing processes and quality oversight. These changes are 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. In December 2017, we requested a meeting with the FDA to describe our remediation efforts and NDA resubmission plans and to seek feedback. A meeting was granted in January 2018, and we believe that the preliminary written responses from the FDA to our questions fully addressed our meeting objectives. We decided that the meeting would no longer be necessary because of the completeness of the FDA's response and that the FDA's comments have not required any substantial change in our manufacturing or regulatory plans. As a result, the correspondence with the FDA will represent the official record of that previously scheduled meeting. Subject to satisfactorily addressing the FDA inspectional observations and demonstrating consistency in our commercial stage manufacturing process, we plan to resubmit our NDA for DEXTENZA for the treatment of post-surgical ocular pain in the first half of 2018. Adequate resolution of the outstanding Form 483 inspectional observations and the final decision as to the adequacy of our manufacturing processes are determined by the FDA with input from CDER's Office of Process and Facilities, as part of the NDA review process, and are necessary prior to NDA approval. If we are unable to resolve these inspectional observations in a timely manner or achieve consistency in our commercial stage manufacturing process, our resubmission of our NDA and its potential approval would be delayed or prevented.

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 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 $16.4 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 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 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 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 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 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 ReSure Sealant has 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.

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 cannot yet accurately predict whether it will it 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 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 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 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, if it is approved for marketing, 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 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 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 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 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 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 DEXTENZA is approved for marketing, we are considering potential commercialization options for DEXTENZA in the United States, including building our own highly targeted, key account sales force that would focus on ambulatory surgical centers responsible for the largest volumes of cataract surgery. We would also expect to leverage such a sales force by selling ReSure Sealant alongside of DEXTENZA. 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-based 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 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 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. 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. If a substantial number of independent distributors on whom we rely, or any significant independent distributor, were to cease to do business with us within a short period of time, our sales of products sold by such distributor or distributors could be adversely affected. In such a situation, we may need to seek alternative independent distributors. Because of the competition for their services, we may be unable to recruit additional qualified independent distributors to work with us. 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 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 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 product candidates and ReSure Sealant, 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 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 or intravitreal injections.

Because the active pharmaceutical ingredients in our 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 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, extended-delivery product candidates that could compete with our intracanalicular insert 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.

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 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 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, 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 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 candidate to other available therapies. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

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 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, if it receives marketing approval, 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.

Subject to the approval of the NDA resubmission we expect to file with the FDA for DEXTENZA for the treatment of post-surgical ocular pain, we will apply for a transitional pass-through reimbursement status, or C code, for DEXTENZA from the Centers for Medicare and Medicaid Services, or CMS, and expect pricing for DEXTENZA while in pass-through status to be approximately $450 to $500 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 have submitted an application to the CMS for a J code for DEXTENZA 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 product candidate.

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 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 product liability insurance coverage in the aggregate, with a per incident limit of $10.0 million, which 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 ReSure Sealant and any other 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-based 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-based 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-based 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. 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 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 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 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 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 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 product candidates, might lead to additional responsibilities for us with respect to 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 product candidates.

Collaboration agreements may not lead to development or commercialization of 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 product candidates could be delayed and we may need additional resources to develop our product candidates. All of the risks relating to product development, regulatory approval and commercialization described in this Annual Report on Form 10-K 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 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 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 licensed patent portfolio expire between 2017 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 licensed 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 the 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 our licensed patents in our field, other Incept licensees may also have the right to enforce our licensed 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 recently 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 any of our 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, 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 licensor's patent rights are highly uncertain. 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 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 licensed 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 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 any patents that we license. Our licensed 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 licensed 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 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 of ours 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 ReSure Sealant 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 licensed 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 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 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 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 aware of a family of U.S. patent applications and issued patents that expired in approximately December 2015 and which have claims that ReSure Sealant could be considered as having infringed. We believe that the claims of this patent family are subject to a claim of invalidity. 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 are aware of a third-party patent relating to intracanalicular inserts that may relate to, and potentially could be asserted against our intracanalicular insert product candidates, including DEXTENZA and OTX-TP. We believe that the claims of this patent are subject to a claim of invalidity.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent and could be forced to indemnify our customers or collaborators. A finding of infringement could also result in an injunction that prevents us from commercializing our product candidates or forces us to cease some of our business operations. In addition, we may be forced to redesign our 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 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 any patent application 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 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 any patent application restricts our ability to expand our business outside of ophthalmology. In particular, if we determine to pursue a strategy of expanding the use of the hydrogel technology outside of the field of ophthalmology, 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. We may not be able to obtain any such required amendment or new license 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 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 ReSure Sealant in the United States, and have not received approval to market any of our product candidates or to market ReSure Sealant in any jurisdiction outside the United States. 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 ReSure Sealant or any of our other 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 to date of the NDA for DEXTENZA for post-surgical ocular pain, the FDA has 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. However, if the FDA determines as part of its review of our NDA that the temperature excursions and associated protocol deviations compromised any of the results from our completed Phase 3 clinical trials, the FDA may request additional site specific data analyses or even exclude certain study subjects from sites in which the temperature excursions were determined to be significant in duration before considering approval of the NDA.

The FDA has 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. We have corresponded with the FDA regarding these inspectional observations and are working to resolve the issues that have been identified in the Form 483, including the presence of particulate matter in certain manufactured lots of DEXTENZA. In November 2017, we submitted our complete responses to the FDA in an effort to close out the Form 483 deficiencies. Subject to satisfactorily addressing the FDA inspectional observations, we plan to resubmit our NDA for DEXTENZA for the treatment of post-surgical ocular pain in the first half of 2018. However, if we are unable to address such issues successfully or if the FDA determines that the actions we have taken or will take to remediate such 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 product candidates from being marketed abroad.

In order to market and sell 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 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 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 product candidates, which could significantly and materially harm our business.

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

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

The FDA required two post-approval studies as a condition for approval of our premarket approval application, or PMA application, for ReSure Sealant. The first post-approval study, identified as the Clinical PAS, was to confirm that ReSure Sealant can be used safely by physicians in a standard cataract surgery practice and to confirm the incidence of the most prevalent adverse ocular events identified in our pivotal study 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, 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. In December 2015, the CMS denied our application for a tracking or research code for ReSure Sealant commercial use. In cooperation with the FDA, we have identified another option for conducting this registry study while maintaining the objective for linking ReSure Sealant use to the Medicare database through a partnership with a third party. In July 2016, the FDA approved the Device Exposure Registry protocol, which should allow us to complete the study in one to two years. 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. Following review of the results from these post-approval studies, or if we are unable to complete the Device Exposure Registry, any concerns with respect to endophthalmitis that we are unable to address due to the lack of completion of the study. This would negatively affect our ability to commercialize ReSure Sealant.

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 ReSure Sealant and any other 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 are found to be in violation of any of the laws described above or any governmental regulations that apply to us, we 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 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 arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws 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.

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 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 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. Since enactment of the ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. In May 2017, the U.S. House of Representatives passed legislation known as the American Health Care Act of 2017. Thereafter, the Senate Republicans introduced and then updated a bill to replace the ACA known as the Better Care Reconciliation Act of 2017. The Senate Republicans also introduced legislation to repeal the ACA without companion legislation to replace it, and a "skinny" version of the Better Care Reconciliation Act of 2017. In addition, the Senate considered proposed healthcare reform legislation known as the Graham-Cassidy bill. None of these measures was passed by the U.S. Senate.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. In January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In October 2017, the President signed a second Executive Order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the ACA exchanges. At the same time, the Administration announced that it will discontinue the payment of cost-sharing reduction, or CSR, payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain.

More recently, 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. Further, each chamber of the Congress has put forth multiple bills designed to repeal or repeal and replace portions of the ACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the ACA. The Congress will likely consider other legislation to replace elements of the ACA, during the next Congressional session.

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 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.

Moreover, legislative and regulatory proposals have also been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical drugs. 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 drug candidates, if any, may be. In addition, increased scrutiny by the United States Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as

subject us and any future collaborators to more stringent drug 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 recently passed comprehensive tax reform bill could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law new legislation that significantly revises the Internal Revenue Code of 1986, as amended. The newly enacted federal income tax law, 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%, limitation of the tax deduction for net interest expense to 30% of adjusted earnings (except for certain small businesses), 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), one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, 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 modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain how various states will respond to the newly enacted federal tax law. The impact of this tax reform 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 this legislation 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, 2017, we had federal and state net operating loss carryforwards of $126.2 million, which begin to expire in 2026, and state net operating loss carryforwards of $109.3 million, which begin to expire in 2026. As of December 31, 2017, we also had federal research and development tax credit carryforwards of $5.5 million and state research and development tax credit carryforwards $2.8 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 newly enacted federal income tax law, 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 newly enacted federal tax law. 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 Executive 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 recently had a reduction in workforce 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 following the planned resubmission of our NDA for 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 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.

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 ReSure Sealant and any product candidates, including potentially DEXTENZA, for which we obtain marketing approval;
- the outcome of our NDA filing for DEXTENZA for the treatment of post-surgical ocular pain;
- 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 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.

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 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 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 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 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.

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 the reduced disclosure requirements applicable to emerging growth 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 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 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 June 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 have been 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). Motions to consolidate these three actions and appoint lead plaintiff(s) for the consolidated action are currently pending.

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 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. Sawney 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.

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, 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 the same defendants and is premised on substantially similar allegations as the previous *Corwin* and *Madera* complaints, and asserts claims for breach of fiduciary duty against the individual defendants and unjust enrichment against the two SV entity defendants. The response to the consolidated complaint is due on April 17, 2018.

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, but does not name either SV Life Sciences Fund, IV, LP or SV Life Sciences Fund IV Strategy Partners, LP as a defendant. The complaint purports to assert derivative claims against the individual defendants for breach of fiduciary duty 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 seeks declaratory, equitable and monetary relief, an unspecified amount of damages, with interest, and attorneys' fees and costs.

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, 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.

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. 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. The following table sets forth the high and low intraday sale prices per share for our common stock on the Nasdaq Global Market for the periods indicated:

2016	High	Low
First Quarter	$ 10.19	$ 5.07
Second Quarter	$ 14.50	$ 4.63
Third Quarter	$ 8.23	$ 4.04
Fourth Quarter	$ 11.91	$ 4.82
2017		
First Quarter	$ 10.49	$ 6.18
Second Quarter	$ 11.79	$ 7.42
Third Quarter	$ 11.00	$ 5.04
Fourth Quarter	$ 6.47	$ 3.30

Holders

As of March 1, 2018, there were approximately 39 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

Dividends

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

Securities Authorized for Issuance under Equity Compensation Plans

The information required by this item will be set forth in our Proxy Statement for the 2018 Annual Meeting of Stockholders and is incorporated in this Annual Report on Form 10-K by reference.

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, 2017 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

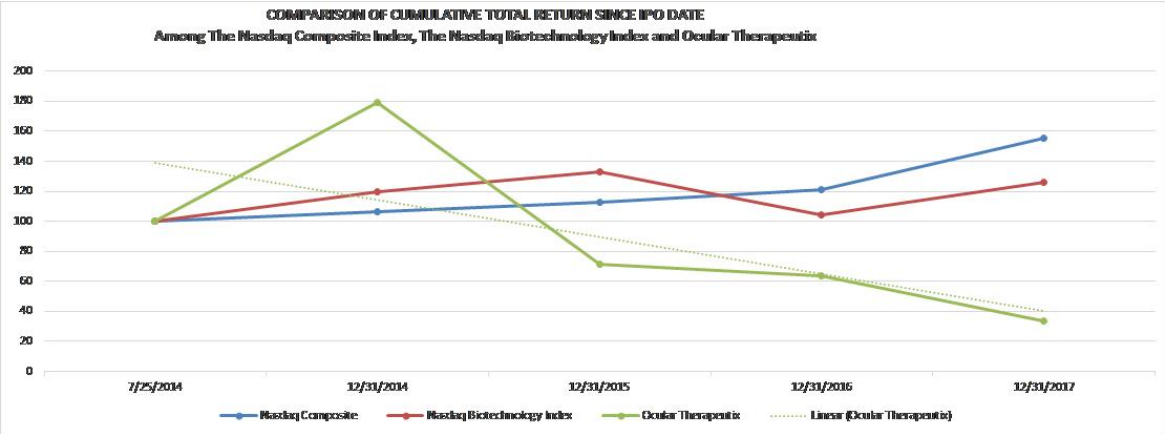
We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

Performance Graph

The following performance graph and related information shall not be deemed to be "soliciting material" or to be "filed" with the SEC for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, nor shall such information be incorporated by reference into any future filing under the Exchange Act or Securities Act, except to the extent that we specifically incorporate it by reference into such filing.

The following graph compares the performance of our common stock to the Nasdaq Composite Index and to the Nasdaq Biotechnology Index from July 25, 2014 (the first date that shares of our common stock were publicly traded)

through December 31, 2017. The comparison assumes $100 was invested after the market closed on July 25, 2014 in our common stock and in each of the foregoing indices, and it assumes reinvestment of dividends, if any. The stock price performance included in this graph is not necessarily indicative of future stock price performance.



Item 6. Selected Financial Data

The following selected financial data should be read together with our 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, 2017, 2016, and 2015, and the balance sheet data as of December 31, 2017 and 2016 from our audited 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, 2014 and 2013 and the balance sheet data as of December 31, 2015, 2014 and 2013 from our audited 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,				
	2017	2016	2015	2014	2013
	(in thousands, except per share data)				
Statement of Operations Data:					
Revenue:					
Product revenue	$ 1,923	$ 1,845	$ 1,354	$ 460	$ —
Collaboration revenue	—	42	396	312	—
Total revenue	1,923	1,887	1,750	772	—
Costs and operating expenses:					
Cost of product revenue	457	443	319	91	—
Research and development	30,880	27,065	26,611	18,880	10,517
Selling and marketing	17,000	6,701	3,852	1,982	625
General and administrative	15,509	11,004	9,165	6,913	1,761
Total costs and operating expenses	63,846	45,213	39,947	27,866	12,903
Loss from operations	(61,923)	(43,326)	(38,197)	(27,094)	(12,903)
Other income (expense):					
Interest income	424	304	166	7	13
Interest expense	(1,892)	(1,680)	(1,724)	(1,119)	(441)
Other income (expense), net	5	(1)	7	(442)	14
Total other expense, net	(1,463)	(1,377)	(1,551)	(1,554)	(414)
Net loss	(63,386)	(44,703)	(39,748)	(28,648)	(13,317)
Accretion of redeemable convertible preferred stock to redemption value	—	—	—	(11)	(27)
Net loss attributable to common stockholders	$(63,386)	$(44,703)	$(39,748)	$(28,659)	$(13,344)
Net loss per share attributable to common stockholders, basic and diluted	$ (2.20)	$ (1.80)	$ (1.71)	$ (2.69)	$ (5.11)
Weighted average common shares outstanding, basic and diluted	28,818	24,816	23,244	10,653	2,609

	As of December 31,				
	2017	2016	2015	2014	2013
	(in thousands)				
Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 41,538	$ 68,145	$ 105,064	$ 74,828	$ 17,505
Working capital	29,914	61,598	101,605	70,309	14,672
Total assets	55,431	74,939	110,306	78,193	19,146
Preferred stock warrant liability	—	—	—	—	254
Long-term debt, net of discount, including current portion	18,016	15,643	15,272	14,865	2,457
Redeemable convertible preferred stock	—	—	—	—	74,344
Total stockholders' equity (deficit)	26,147	52,008	89,588	58,696	(59,472)

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 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 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 extended delivery of drug to the eye. We believe that our extended delivery technology allows us 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 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.

Our lead product candidates are DEXTENZA (dexamethasone insert), for the treatment of post-surgical ocular pain and inflammation, allergic conjunctivitis and dry eye disease, and OTX-TP (travoprost insert), for the reduction of intraocular pressure, or IOP, in patients with glaucoma and ocular hypertension. Both product candidates are extended-delivery, drug-eluting, preservative-free intracanalicular inserts that are placed into the canaliculus through a natural opening called the punctum located in the inner portion of the eyelid near the nose. We also have a preclinical product development candidate that is injected into the intracameral space for the reduction of IOP in patients with glaucoma and ocular hypertension where greater IOP reduction is needed.

We also have in development two programs that are beginning human clinical trials: OTX-TIC, an intracameral travoprost implant for the reduction of IOP in patients with moderate to severe glaucoma and ocular hypertension; and OTX-TKI, a tyrosine kinase inhibitor intravitreal injection by fine gauge needle, delivering a hydrogel-based, anti-angiogenic formulation that releases the therapeutic agent for the treatment of wet AMD. Currently, we have not enrolled a patient in either program. Finally, we continue our 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 our sole commercial product ReSure Sealant, a hydrogel-based 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™ (dexamethasone insert)

Our most advanced product candidate, DEXTENZA, incorporates the FDA-approved corticosteroid dexamethasone as an active pharmaceutical ingredient into a hydrogel-based, drug-eluting intracanalicular insert. In September 2015, we submitted to the FDA a New Drug Application, or NDA, for DEXTENZA for the treatment of post-surgical ocular pain. In July 2016, we received a Complete Response Letter, or CRL, from the FDA regarding our NDA for DEXTENZA. 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. 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. FDA concerns included deficiencies in manufacturing processes and analytical testing related to manufacturing of drug product identified during the pre-NDA approval inspection and states that the FDA has determined that it cannot approve the NDA in its present form. We have corresponded with the FDA regarding these inspectional observations and are working to resolve the issues that have been identified. 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.

Subject to satisfactorily addressing the FDA inspectional observations and demonstrating consistency in our commercial stage manufacturing process, we plan to resubmit our NDA for DEXTENZA for the treatment of post-surgical ocular pain in the first half of 2018. Adequate resolution of the outstanding Form 483 inspectional observations and the final decision as to the adequacy of our manufacturing processes are determined by the FDA with input from the Office of Process and Facilities within its Center for Drug Evaluation and Research, or CDER, as part of the NDA review process, and are necessary prior to NDA approval.

If DEXTENZA is approved for marketing, we are considering potential commercialization options available for DEXTENZA in the United States, including building our own highly targeted, key account sales force that would focus on the ambulatory surgical centers responsible for the largest volumes of cataract surgery.

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 are being used to support our NDA for post-surgical ocular pain. Subject to receiving approval for the pain indication, we plan to submit an NDA supplement, or sNDA, for DEXTENZA for the treatment of post-surgical ocular inflammation. We have also 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. Finally, DEXTENZA completed a Phase 2 clinical trial for the treatment of dry eye disease, with topline results announced in December 2015.

OTX-TP (travoprost insert)

Our second product candidate, OTX-TP, incorporates travoprost, an FDA-approved prostaglandin analog, or PGA, that reduces elevated IOP as its active pharmaceutical ingredient, into a hydrogel-based, 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 mild to moderate 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 Phase 3 clinical trials of OTX-TP in September 2016 and initiated the first of two Phase 3 clinical trials of OTX-TP in September 2016. We expect our first Phase 3 trial to enroll approximately 550 patients at 50 sites in the United States. Based on discussions with the FDA, the first Phase 3 clinical trial design will include an OTX-TP treatment arm and a placebo-controlled comparator arm that will use a non-drug eluting hydrogel-based intracanalicular insert. There will not be a requirement for either a timolol comparator or a validation arm. No eye drops, placebo or active, will be administered in either the OTX-TP treatment arm or the placebo-controlled arm. The primary efficacy endpoint will be 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 fourth quarter of 2018. We do not intend to initiate the second Phase 3 clinical trial until we receive data from the first Phase 3 clinical trial and may determine to discuss 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 will need to generate six-month (300 patients) and one year (100 patients) safety data during either the first or second Phase 3 clinical trial to support our product registration.

OTX-TIC (travoprost implant)

OTX-TIC (travoprost implant) is our product candidate for the treatment of patients with moderate to severe glaucoma 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 lowering in humans. We initiated a Phase 1 clinical trial outside the United States in third quarter of 2017 to assess safety and obtain initial efficacy data. The trial is a prospective, single-center study designed to evaluate the safety, efficacy, durability and tolerability of OTX-TIC compared to topical travoprost (eye drops) in up to 20 patients with open-angle glaucoma or ocular hypertension. We submitted an investigational new drug application, or IND, in the first quarter of 2018 and expect to initiate a second Phase 1 trial in the United States in the first half of 2018.

Back-of-the-Eye Programs

We are engaged in the preclinical 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 of a protein-based large molecule or small molecule TKI drug targeting VEGF over a four to six month period of a protein-based large molecule or small molecule TKI drug, 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 (tyrosine kinase inhibitor implant)

OTX-TKI *(*tyrosine kinase inhibitor implant*)* 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. We plan to initiate a Phase 1 clinical trial outside the United States in the first half of 2018 to assess the safety, durability and tolerability of OTX-TKI in the posterior segment of the human eye for the treatment of VEGF induced retinal leakage for an extended duration.

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.

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

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 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 new areas of the body. If we are to utilize our intellectual property, all of which we currently license from Incept, LLC, or Incept, for applications outside the field of ophthalmology, we will 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.

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 sustained 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 $63.4 million, $44.7 million and $39.7 million for the years ended December 31, 2017, 2016 and 2015, respectively. As of December 31, 2017, we had an accumulated deficit of $237.3 million.

Our total cost and operating expenses were $63.8 million, $45.2 million and $39.9 million for the years ended December 31, 2017, 2016 and 2015, respectively, including $7.3 million, $6.0 million and $4.6 million, respectively, in non-cash stock-based compensation expense. Our operating expenses have grown as we continue to pursue the clinical development of our most advanced product candidates, DEXTENZA and OTX-TP; continue the research and development of our other product candidates; continue the internal development of our intravitreal hydrogel-based formulation for the sustained delivery of protein-based or small molecule anti-angiogenic drugs, such as anti-VEGF drugs and TKIs 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 lower sales and marketing expenses for our product candidates until we obtain marketing approval of DEXTENZA or any of our other product candidates. In addition, we will continue to incur additional costs associated with operating as a public company.

We do not expect to generate significant revenue from sales of any product for several years, if at all. Accordingly, we may need to obtain substantial additional funding in connection with our continuing operations. 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.

In July 2014, we completed an initial public offering, or IPO, of our common stock, 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 of our 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 an At-the-Market Sales Agreement, or the 2016 ATM Agreement with Cantor Fitzgerald & Co., or Cantor, under which we may offer and sell our common stock having aggregate proceeds of up to $40.0 million from time to time. Through January 31, 2018, we have sold an aggregate of 890,568 shares of common stock under the 2016 ATM Agreement resulting in net proceeds of approximately $6.6 million after underwriting discounts, commission and other offering expenses. 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. Based on our current plans and forecasted expenses, we believe that our existing cash and cash equivalents, as of December 31, 2017, along with the proceeds from our public offering of common stock in January 2018 but 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 through the first quarter of 2019. 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. We have not reflected the full costs of building a sales force that we would build if DEXTENZA is approved for marketing in our current operating plan and will need to raise additional capital to support such an effort. See "—Liquidity and Capital Resources."

Financial Operations Overview

Revenue

From our inception through December 31, 2017, 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 2018. 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.

We entered into a feasibility agreement with a biotechnology company relating to our intravitreal drug delivery injection in October 2014. Under this agreement, the biotechnology company had agreed to pay us up to $0.7 million, of which $0.3 million was a non-refundable up-front payment due upon contract execution and $0.4 million will be due upon the achievement of certain milestones. Initially, we were recognizing the non-refundable, non-contingent up-front payment of $0.3 million as revenue on a straight-line basis over the twelve-month period in which we are expected to complete our performance obligations. Estimates of this development period involves the evaluation of many assumptions and uncertainties and may change if facts and circumstances change. During 2015, management reevaluated and revised the estimated development period to extend through March 2016. If and when a contingent milestone payment is earned, the additional consideration to be received will be added to the total expected payments under the contract and recognized as revenue based on the proportional performance methodology. In January 2015, we achieved

the first milestone under the feasibility agreement triggering a payment due of $0.3 million. This agreement was terminated in the second quarter of 2016 and the Company does not have any further obligations.

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,		
	2017	2016	2015
	(in thousands)		
ReSure Sealant	$ 126	$ 236	$ 330
DEXTENZA for post-surgical ocular pain and inflammation	1,319	2,686	2,058
DEXTENZA for allergic conjunctivitis	621	2,815	5,541
DEXTENZA for dry eye disease	6	101	662
OTX-TP for glaucoma and ocular hypertension	5,288	1,941	2,048
Unallocated expenses	23,520	19,286	15,972
Total research and development expenses	$30,880	$27,065	$26,611

We expect that our expenses will increase in connection with our ongoing activities. We estimate that in 2018, we will incur approximately $38.0 million to $40.5 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 $28.0 million to $29.0 million of external research and development expenses related to clinical trial and regulatory costs for our DEXTENZA and OTX-TP product candidates and approximately $10.0 million to $11.0 million of other research and development activities that we do not expect to track by program. In addition, we expect to purchase $1.5 million to $2.0 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 2018, as follows:

- approximately $8.0 million to $8.5 million for DEXTENZA for post-surgical ocular pain and inflammation;
- approximately $14.0 million to $14.5 million for OTX-TP for glaucoma and ocular hypertension;
- approximately $6.0 million to $6.5 million for OTX-TKI for Wet AMD; and
- approximately $10.0 million to $11.0 million for other external research and development activities.

The successful development and commercialization of our 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 product candidates compared to alternative treatments, including any standard of care;
- the market acceptance of our 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, 2017, 2016 and 2015, we incurred selling and marketing expense in connection with ReSure Sealant, which we began commercializing in the first quarter of 2014.

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. As a result, we expect our selling and marketing expenses to decrease until we obtain marketing approval of our product candidates.

Other Income (Expense)

Interest income consists primarily of interest income earned on cash and cash equivalents. In each of 2017, 2016, and 2015, 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.

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 2015, 2016 and 2017, 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 financial statements are prepared in accordance with generally accepted accounting principles in the United States of America. The preparation of our 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 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 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 financial statements.

Revenue Recognition

We recognize revenue when the following four criteria are met in accordance with Accounting Standards Codification, or ASC, 605, Revenue Recognition: persuasive evidence of a sales arrangement exists; delivery of goods has occurred through transfer of title and risk and rewards of ownership; the selling price is fixed or determinable; and collectability is reasonably assured.

We record revenue from product sales net of applicable provisions for returns, chargebacks, discounts, wholesaler management fees, government and commercial rebates, and other applicable allowances in the same period in which the related sales are recorded, based on the underlying contract terms.

We analyze multiple-element arrangements based on the guidance in ASC Topic 605-25, Revenue Recognition—Multiple-Element Arrangements, or ASC 605-25. Pursuant to this guidance, we evaluate multiple-element arrangements to determine (1) the deliverables included in the arrangement and (2) whether the individual deliverables represent separate units of accounting or whether they must be accounted for as a combined unit of accounting. This evaluation involves subjective determinations and requires us to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that the delivered item has value to the customer on a standalone basis and, if the arrangement includes a general right of return relative to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in our control. In assessing whether an item has standalone value, we consider factors such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, we consider whether the collaboration partner can use the other deliverables for their intended purpose without the receipt of the remaining elements, whether the value of the deliverable is dependent on the undelivered item and whether there are other vendors that can provide the undelivered elements.

We allocate arrangement consideration that is fixed or determinable among the separate units of accounting using the relative selling price method. Then, we apply the applicable revenue recognition criteria in ASC 605 to each of the separate units of accounting in determining the appropriate period and pattern of recognition. We determine the selling price of a unit of accounting following the hierarchy of evidence prescribed by ASC 605-25. Accordingly, we determine the estimated selling price for units of accounting within each arrangement using vendor-specific objective evidence, or VSOE, of selling price, if available; third-party evidence, or TPE, of selling price, if VSOE is not available; or best estimate of selling price, or BESP, if neither VSOE nor TPE is available. We typically use BESP to estimate the selling price as we generally do not have VSOE or TPE of selling price for our units of accounting. Determining the BESP for a unit of accounting requires significant judgment. In developing the BESP for a unit of accounting, we consider applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with our customer and estimated costs. We validate the BESP for units of accounting by evaluating whether changes in the key assumptions used to determine the BESP will have a significant effect on the allocation of arrangement consideration between multiple units of accounting.

We recognize arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria in ASC 605 are satisfied for that particular unit of accounting. We will recognize as revenue arrangement consideration attributed to licenses that have standalone value relative to the other deliverables to be provided in an arrangement upon delivery. We will recognize as revenue arrangement consideration attributed to licenses that do not have standalone value relative to the other deliverables to be provided in an arrangement over our estimated performance period, as the arrangement would be accounted for as a single unit of accounting.

At the inception of an arrangement that includes milestone payments, we evaluate whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether: (1) the consideration is commensurate with either our performance to achieve the milestone or the enhancement of the value of the delivered item as a result of a specific outcome resulting from our performance to achieve the milestone, (2) the consideration relates solely to past performance, and (3) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. We evaluate factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the respective milestone and the level of effort and investment required to achieve the respective milestone in making this assessment. There is considerable judgment involved in determining whether a milestone satisfies all of the criteria required to conclude that a milestone is substantive. Accordingly, pursuant to the guidance of ASC Topic 605-28, Revenue Recognition—Milestone Method, or ASC 605-28, revenue from milestone payments will be recognized in its entirety upon successful accomplishment of the milestone, assuming all other revenue recognition criteria are met.

Other contingent, event-based payments received for which payment is either contingent solely upon the passage of time or the results of a collaborative partner's performance would not be considered milestones under ASC 605-28. In accordance with ASC 605-25, such payments will be recognized as revenue when all of the four basic revenue recognition criteria are met.

Whenever we determine that an element is delivered over a period of time, revenue is recognized using either a proportional performance model or a straight-line model over the period of performance. At each reporting period, we reassess our cumulative measure of performance and make appropriate adjustments, if necessary. We recognize revenue using the proportional performance model whenever we can make reasonably reliable estimates of the level of effort required to complete our performance obligations under an arrangement. Revenue recognized under the proportional performance model at each reporting period is determined by multiplying the total expected payments under the contract (excluding payments contingent upon achievement of milestones) by the ratio of the level of effort incurred to date to the estimated total level of effort required to complete the performance obligations under the arrangement. Revenue is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the proportional performance model as of each reporting period. Alternatively, if we cannot make reasonably reliable estimates the level of effort required to complete our performance obligations under an arrangement, then revenue under the arrangement is recognized on a straight-line basis over the period expected to complete our performance obligations. If and when a contingent milestone payment is earned, the additional consideration to be received is added to the total expected payments under the contract. Revenue is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined on a straight-line basis as of the period end date. If we cannot reasonably estimate when our performance obligation period ends, then revenue is deferred until we can reasonably estimate when the performance obligation period ends.

Accrued Research and Development Expenses

As part of the process of preparing our 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 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:

	Year Ended December 31,		
	2017	2016	2015
Risk-free interest rate	2.00 %	1.42 %	1.67 %
Expected term (in years)	6	6	6
Expected volatility	102 %	85 %	71 %
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.

Inventory Valuation

Inventory is valued at the lower of cost or market, determined by the first-in, first-out method. Prior to initial approval by the FDA or other regulatory agencies of our products, we expense costs relating to the production of inventory in the period incurred as research and development expenses. After such time as the product receives approval, we begin to capitalize the inventory costs related to the product.

JOBS Act

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.

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, 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	1,923	1,887	36
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	63,846	45,213	18,633
Loss from operations	(61,923)	(43,326)	(18,597)
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	(1,463)	(1,377)	(86)
Net loss	$(63,386)	$(44,703)	$(18,683)

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

	Year Ended December 31,		Increase (Decrease)
	2017	2016	
	(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	$30,880	$27,065	$ 3,815

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 the DEXTENZA product candidate 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 our DEXTENZA product candidate for the treatment of post-surgical ocular pain and inflammation which was in Phase 3 clinical trials, $0.6 million for our DEXTENZA product candidate 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 our DEXTENZA product candidate for the treatment of allergic conjunctivitis which was in Phase 3 clinical trials and $2.7 million for our DEXTENZA for ocular pain and inflammation following cataract surgery which was in Phase 3 clinical trials and $0.1 million for our DEXTENZA product candidate 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

	Year Ended December 31,		Increase (Decrease)
	2017	2016	
	(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	$17,000	$ 6,701	$10,299

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. As a result, we expect our selling and marketing expenses to decrease until we obtain marketing approval of our product candidates.

General and Administrative Expenses

	Year Ended December 31,		Increase (Decrease)
	2017	2016	
	(in thousands)		
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	$15,509	$11,004	$ 4,505

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.

Comparison of the Years Ended December 31, 2016 and December 31, 2015

The following table summarizes our results of operations for the years ended December 31, 2016 and 2015:

	Year Ended December 31,		Increase (Decrease)
	2016	2015	
	(in thousands)		
Revenue:			
Product revenue	$ 1,845	$ 1,354	$ 491
Collaboration revenue	42	396	(354)
Total revenue	1,887	1,750	137
Costs and operating expenses:			
Cost of product revenue	443	319	124
Research and development	27,065	26,611	454
Selling and marketing	6,701	3,852	2,849
General and administrative	11,004	9,165	1,839
Total costs and operating expenses	45,213	39,947	5,266
Loss from operations	(43,326)	(38,197)	(5,129)
Other income (expense):			
Interest income	304	166	138
Interest expense	(1,680)	(1,724)	44
Other income (expense), net	(1)	7	(8)
Total other expense, net	(1,377)	(1,551)	174
Net loss	$ (44,703)	$ (39,748)	$ (4,955)

Revenue

We generated $1.8 and $1.4 million of product revenue during the years ended December 31, 2016 and December 31, 2015, 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 2016. We generated $42,000 and $0.4 million of revenue from our collaboration agreements in 2016 and 2015, respectively.

Research and Development Expenses

	Year Ended December 31, 2016	2015	Increase (Decrease)
	(in thousands)		
Direct research and development expenses by program:			
ReSure Sealant	$ 236	$ 330	$ (94)
DEXTENZA for post-surgical ocular pain and inflammation	2,686	2,058	628
DEXTENZA for allergic conjunctivitis	2,815	5,541	(2,726)
DEXTENZA for dry eye disease	101	662	(561)
OTX-TP for glaucoma and ocular hypertension	1,941	2,048	(107)
Unallocated expenses:			
Personnel costs	11,630	9,345	2,285
All other costs	7,656	6,627	1,029
Total research and development expenses	$27,065	$26,611	$ 454

Research and development expenses were $27.1 million for the year ended December 31, 2016, compared to $26.6 million for the year ended December 31, 2015. The increase of $0.4 million was primarily due to a decrease of $2.9 million in clinical trial and regulatory expenses and an increase of $3.3 million in unallocated expenses. Clinical trial and regulatory expenses decreased in the year ended December 31, 2016, compared to the year ended December 31, 2015 primarily due to the timing and number of clinical trials being conducted for the DEXTENZA product candidate for the treatment of allergic conjunctivitis and dry eye disease.

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 $2.7 million for our DEXTENZA product candidate for the treatment of post-surgical ocular pain and inflammation which was in Phase 3 clinical trials, $2.8 million for our DEXTENZA product candidate for the treatment of allergic conjunctivitis which was in Phase 3 clinical trials, $0.1 million for our DEXTENZA product candidate for the treatment of dry eye disease which was in Phase 2 clinical trials, and $2.0 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, 2015, we incurred $10.3 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 2b clinical trials, $5.5 million for our DEXTENZA product candidate for the treatment of allergic conjunctivitis which was in Phase 3 clinical trials and $2.1 million for our DEXTENZA product candidate for ocular pain and inflammation following cataract surgery which was in Phase 3 clinical trials and $0.7 million for our DEXTENZA product candidate for the treatment of dry eye disease which was in Phase 2 clinical trials. Unallocated research and development costs increased $3.3 million for the year ended December 31, 2016, compared to the year ended December 31, 2015 primarily due to an increase in unallocated personnel costs of $2.3 million, relating to additional hiring primarily in our clinical, regulatory and quality department, an increase in stock-based compensation expense and the write off of $1.3 million of equipment that was in construction in process that is included in all other costs.

Selling and Marketing Expenses

	Year Ended December 31, 2016	2015	Increase (Decrease)
	(in thousands)		
Personnel related (including stock-based compensation)	$ 2,580	$ 1,508	$ 1,072
Professional fees	2,993	1,625	1,368
Facility related and other	1,128	719	409
Total selling and marketing expenses	$ 6,701	$ 3,852	$ 2,849

Selling and marketing expenses were $6.7 million for the year ended December 31, 2016, compared to $3.9 million for the year ended December 31, 2015. The increase of $2.8 million was primarily due to an increase of $1.1 million in personnel costs relating to additional hiring as we planned for the potential launch of DEXTENZA and additional stock-based compensation expense, an increase of $1.4 million in professional fees due to increased spending on consulting, trade shows and conferences and an increase of $0.4 million in facility-related and other costs.

General and Administrative Expenses

	Year Ended December 31, 2016	2015	Increase (Decrease)
	(in thousands)		
Personnel related (including stock-based compensation)	$ 6,184	$ 5,216	$ 968
Professional fees	3,732	2,951	781
Facility related and other	1,088	998	90
Total general and administrative expenses	$ 11,004	$ 9,165	$ 1,839

General and administrative expenses were $11.0 million for the year ended December 31, 2016, compared to $9.2 million for the year ended December 31, 2015. The increase of $1.8 million was due to a $1.0 million increase in personnel related costs, an increase of $0.8 million in professional fees, and an increase of $0.1 million in facility-related and other costs. Our personnel related costs increased primarily due to an increase in stock compensation expense of $0.9 million. Professional fees increased primarily due to activities to support our operating as a public company.

Other Income (Expense), Net

Other expense, net was $1.4 million for the year ended December 31, 2016, compared to $1.6 million for the year ended December 31, 2015.

Liquidity and Capital Resources

Since inception, we have incurred significant operating losses. Our net losses were $63.4 million, $44.7 million and $39.7 million for the years ended December 31, 2017, 2016 and 2015, respectively. As of December 31, 2017, we had an accumulated deficit of $237.3 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 sustained 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.

Through December 31, 2017, 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 ATM Agreement with Cantor, under which we may offer and sell our common stock having aggregate proceeds of up to $40.0 million from time to time. To date, we have sold 890,568 shares of common stock under the 2016 ATM Agreement resulting in net proceeds of approximately $6.6 million after underwriting discounts, commission and other offering expenses. 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, 2017, we had cash and cash equivalents of $41.5 million. In January 2018, we completed a follow-on offering of our common stock and received net proceeds from the offering of $35.1 million.

As of December 31, 2017, we had outstanding debt of $18.0 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. See "—Contractual Obligations and Commitments" for additional information.

Cash Flows

As of December 31, 2017, we had cash and cash equivalents of $41.5 million and outstanding debt of $18.0 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, 2017, along with the proceeds from our public offering of common stock in January 2018 but 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 through the first quarter of 2019. 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. We have not reflected the full costs of building a sales force that we would build if DEXTENZA is approved for marketing in our current operating plan and will need to raise additional capital to support such an effort. 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:

	Year Ended December 31,		
	2017	2016	2015
	(in thousands)		
Cash used in operating activities	$(50,473)	$(34,001)	$(33,743)
Cash provided by investing activities	27,067	35,568	(38,569)
Cash provided by (used in) financing activities	32,008	585	65,703
Net increase in cash and cash equivalents	$ 8,602	$ 2,152	$ (6,609)

Operating activities. 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.

Net cash used in operating activities was $33.7 million for the year ended December 31, 2015, primarily resulting from our net loss of $39.7 million, partially offset by non-cash charges of $5.6 million and cash provided by changes in our operating assets and liabilities of $0.5 million. Our net loss was primarily attributed to research and development activities and our general and administrative expenses partially offset by $1.8 million of revenue in the period. Our net non-cash charges during the year ended December 31, 2015 primarily consisted of $4.6 million of stock-based compensation expense and $0.8 million of depreciation expense. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2015 consisted primarily of a $0.2 million increase in accrued expenses and deferred rent and a $0.3 million increase in accounts payable, which was due to the timing of vendor invoicing and payments, both partially offset by a decrease in accounts receivable of $0.1 million.

Investing activities. 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. Net cash used in investing activities for the year ended December 31, 2015 consisted of cash used to purchase property and equipment of $1.8 million and cash used to purchase marketable securities of $91.7 million offset by maturities of marketable securities of $54.8 million.

Financing activities. 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 ATM 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 ATM 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. Net cash provided by financing activities for 2015 was $65.7 million and consisted primarily of proceeds of $65.6 million, net of underwriting discounts and other offering expenses, related to our follow-on offering, $1.5 million (net) in borrowings under our amended 2014 credit facility, 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 $0.2 million partially offset by repayment of $1.5 million of outstanding principal under our 2014 credit facility, payments of $0.8 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:

- continue to pursue the clinical development of our most advanced intracanalicular insert product candidates, DEXTENZA and OTX-TP;
- commence 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-based 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;
- seek marketing approvals for any of our product candidates that successfully complete clinical development;
- develop and expand our sales, marketing and distribution capabilities for any of our product candidates, including DEXTENZA, for which we may obtain marketing approval;
- 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;
- 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, 2017, along with the proceeds from our public offering of common stock in January 2018 but 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 through the first quarter of 2019. 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. We have not reflected the full costs of building a sales force that we would build if DEXTENZA is approved for marketing in our current operating plan and will need to raise additional capital to support such an effort.

Our future capital requirements will depend on many factors, including:

- the costs, timing and outcome of regulatory review of our product candidates by the FDA, the EMA or other regulatory authorities, including the resubmission of our NDA for DEXTENZA;
- the level of product sales from 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 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 DEXTENZA and OTX-TP;

- 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-based 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 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 outcome of certain 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 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 will enable us to meet our planned operational expenses, debt service obligations, and capital expenditures, based on our current operating plans, only through the first quarter of calendar year 2019, 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, 2017, we had federal net operating loss carryforwards of $126.2 million, which begin to expire in 2026, and state net operating loss carryforwards of $109.3 million, which begin to expire in 2026. As of December 31, 2017, we also had federal research and development tax credit carryforwards of $5.5 million and state research and development tax credit carryforwards $2.8 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, 2017 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	$ 16,149	$ 1,715	$ 3,657	$ 4,177	$ 6,600
Purchase commitments	2,372	2,372	—	—	—
Facility improvements, net	282	282	—	—	—
Manufacturing commitments	1,680	—	1,680	—	—
Debt obligations including interest	21,015	6,965	14,050	—	—
Total	$ 41,498	$11,334	$19,387	$ 4,177	$ 6,600

In the table above, we set forth our enforceable and legally binding obligations and future commitments at December 31, 2017, 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, 2017. 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 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, we have billed the landlord for $2.7 million and received payments of $2.6 million from the landlord. We have 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. There are 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. The obligations under the credit 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 credit facility is secured by substantially all of our assets except for our intellectual property, which is subject to a negative pledge.

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 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 million, which cap may be increased by up to $5 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.

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 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, 2017, we had cash and cash equivalents of $41.5 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 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, 2017. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the 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, 2017, 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 Securities Exchange Act of 1934 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 assessed the effectiveness of our internal control over financial reporting as of December 31, 2017. 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, 2017, 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, 2017 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 2018 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 2018 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 2018 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 2018 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 2018 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 2018 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 2018 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 2018 Annual Meeting of Stockholders and is incorporated in this Annual Report on Form 10-K by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules

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

No financial statement schedules have been filed as part of this Annual Report on Form 10-K because they are not applicable, not required or because the information is otherwise included in our 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 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				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
3.1	Restated Certificate of Incorporation of the Registrant	8-K	001-36554	7/30/2014	3.1	
3.2	Amended and Restated Bylaws of the Registrant	8-K	001-36554	7/30/2014	3.2	
4.1	Specimen Stock Certificate evidencing the shares of common stock	S-1/A	333-196932	7/11/2014	4.1	
10.1+	2006 Stock Incentive Plan, as amended	S-1	333-196932	6/20/2014	10.1	
10.2+	Form of Stock Option Agreement under 2006 Stock Incentive Plan	S-1	333-196932	6/20/2014	10.2	
10.3+	Form of Restricted Stock Agreement under 2006 Stock Incentive Plan	S-1	333-196932	6/20/2014	10.3	
10.4+	2014 Stock Incentive Plan	S-1/A	333-196932	7/11/2014	10.4	
10.5+	Form of Incentive Stock Option Agreement under 2014 Stock Incentive Plan	S-1/A	333-196932	7/11/2014	10.5	
10.6+	Form of Non-statutory Stock Option Agreement under 2014 Stock Incentive Plan	S-1/A	333-196932	7/11/2014	10.6	
10.7+	Form of Restricted Stock Agreement under 2014 Stock Incentive Plan	S-1/A	333-196932	7/11/2014	10.7	
10.8†	Amended and Restated License Agreement, dated January 27, 2012, between the Registrant and Incept LLC	S-1	333-196932	6/20/2014	10.8	
10.9	Lease Agreement dated September 2, 2009, by and between the Registrant and RAR2-Crosby Corporate Center QRS, Inc., as amended.	S-1	333-196932	6/20/2014	10.9	
10.10+	2014 Employee Stock Purchase Plan	S-1/A	333-196932	7/11/2014	10.10	
10.11	Form of Indemnification Agreement by and between the Registrant and each of its directors and executive officers	S-1	333-196932	6/20/2014	10.12	
10.12+	Amended and Restated Employment Agreement, dated June 24, 2014, by and between the Registrant and Amarpreet S. Sawhney, Ph.D.	S-1/A	333-196932	7/11/2014	10.13	

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
10.13+	Employment Agreement, dated June 19, 2014, by and between the Registrant and James Fortune	S-1/A	333-196932	7/11/2014	10.15	
10.14+	Employment Agreement, dated July 3, 2014, by and between the Registrant and Eric Ankerud	S-1/A	333-196932	7/11/2014	10.16	
10.15	Amended and Restated Credit and Security Agreement, by and among Midcap Funding III Trust, Silicon Valley Bank, Flexpoint MCLS SPV LLC, and the Registrant	8-K	001-36554	12/9/2015	10.1	
10.16	Lease Agreement dated June 17, 2016 between the WS NF 15 Crosby Drive, LLC and the Registrant	10-Q	001-36554	8/9/2016	10.1	
10.17	First Amendment dated June 20, 2016 to Amended and Restated Credit and Security Agreement among MidCap Funding III Trust, Silicon Valley Bank, Flexpoint MCLS SPV LLC and the Registrant	10-Q	001-36554	8/9/2016	10.2	
10.18†	Collaboration, Option and License Agreement between Ocular Therapeutix, Inc. and Regeneron Pharmaceuticals, Inc. dated October 10, 2016	10-Q	001-36554	11/9/2016	10.1	
10.19	Controlled Equity Offering Sales Agreement, dated November 29, 2016, by and between Ocular Therapeutix, Inc. and Cantor Fitzgerald & Co.	8-K	001-36554	11/30/2016	1.1	
10.20	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	10-Q	001-36554	5/5/2017	10.1	
10.21+	Amendment to Employment Agreement, by and between the registrant and Amarpreet S. Sawhney, dated as of June 20, 2017	8-K	001-36554	6/22/2017	10.1	
10.22+	Employment Agreement, by and between registrant and Antony C. Mattessich, dated as of June 20, 2017	8-K	001-36554	6/22/2017	10.2	

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
10.23+	Non-Statutory Stock Option Agreement, by and between Ocular Therapeutix, Inc. and Antony C. Mattessich dated as of June 20, 2017	8-K	001-36554	6/22/2017	10.3	
10.24+	Transition, Separation and release of Claims Agreement by and between Ocular Therapeutix, Inc. and Eric Ankerud, dated as of July 31, 2017	8-K	001-36554	8/3/2017	10.1	
10.25	Consulting Agreement by and between Ocular Therapeutix, Inc. and Anchor Biotech Consulting, LLC dated as of July 31, 2017	8-K	001-36554	8/3/2017	10.2	
10.26+	Employment Agreement, by and between Ocular Therapeutix, Inc. and Donald Notman, dated as of September 25, 2017	8-K	001-36554	9/25/2017	10.1	
10.27	Second Amendment to Lease, by and between Ocular Therapeutix, Inc. and CCC Investors LLC, dated October 10, 2017	8-K	001-36554	10/16/2017	10.1	
10.28+	Transition, Separation and release of Claims Agreement by and between Ocular Therapeutix, Inc. and James Fortune, dated as of October 13, 2017	8-K	001-36554	10/13/2017	10.1	
10.29+	Employment Agreement, by and between Ocular Therapeutix, Inc. and Daniel Bollag, dated as of July 31, 2017					X
10.30+	Employment Agreement, by and between Ocular Therapeutix, Inc. and Michael Goldstein, dated as of September 25, 2017					X
10.31+	Employment Agreement, by and between Ocular Therapeutix, Inc. and Kevin Hanley, dated as of January 5, 2018					X
23.1	Consent of PricewaterhouseCoopers LLP					X
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended					X
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended					X
32.1	Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
32.2	Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
101.INS	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 8, 2018

OCULAR THERAPEUTIX, INC.

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

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

Signature	Title	Date
/s/ Antony Mattessich Antony Mattessich	President and Chief Executive Officer (Principal Executive Officer)	March 8, 2018
/s/ Donald Notman Donald Notman	Chief Financial Officer (Principal Financial and Accounting Officer)	March 8, 2018
/s/ Amarpreet Sawhney, Ph.D. Amarpreet Sawhney, Ph.D	Executive Chairman of the Board	March 8, 2018
/s/ Jaswinder Chadha Jaswinder Chadha	Director	March 8, 2018
/s/ Jeffrey S. Heier, M.D. Jeffrey S. Heier, M.D.	Director	March 8, 2018
/s/ Richard L. Lindstrom, M.D. Richard L. Lindstrom, M.D.	Director	March 8, 2018
/s/ William James O'Shea William James O'Shea	Director	March 8, 2018
/s/ Bruce A. Peacock Bruce A. Peacock	Director	March 8, 2018
/s/ Charles Warden Charles Warden	Director	March 8, 2018

OCULAR THERAPEUTIX, INC.

INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of
Ocular Therapeutix, Inc.:

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Ocular Therapeutix, Inc. as of December 31, 2017 and 2016, and the related 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, 2017, including the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2017 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 financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the 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 financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

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

We conducted our audits of these 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 financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

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

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
March 8, 2018

We have served as the Company's auditors since 2008.

OCULAR THERAPEUTIX, INC.

BALANCE SHEETS

(In thousands, except share and per share data)

	December 31, 2017	December 31, 2016
Assets		
Current assets:		
Cash and cash equivalents	$ 41,538	$ 32,936
Marketable securities	—	35,209
Accounts receivable	226	250
Inventory	122	113
Prepaid expenses and other current assets	1,453	1,390
Total current assets	43,339	69,898
Property and equipment, net	10,478	3,313
Restricted cash	1,614	1,728
Total assets	$ 55,431	$ 74,939
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 3,571	$ 2,116
Accrued expenses and deferred rent	4,310	4,635
Notes payable, net of discount, current	5,545	1,549
Total current liabilities	13,426	8,300
Deferred rent, long-term	3,387	537
Notes payable, net of discount, long-term	12,471	14,094
Total liabilities	29,284	22,931
Commitments and contingencies (Note 13)		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 5,000,000 shares authorized at December 31, 2017 and December 31, 2016; no shares issued or outstanding at December 31, 2017 and December 31, 2016	—	—
Common stock, $0.0001 par value; 100,000,000 shares authorized at December 31, 2017 and December 31, 2016; 29,658,202 and 25,024,100 shares issued and outstanding at December 31, 2017 and December 31, 2016, respectively	3	3
Additional paid-in capital	263,409	225,889
Accumulated deficit	(237,265)	(173,879)
Accumulated other comprehensive loss	—	(5)
Total stockholders' equity	26,147	52,008
Total liabilities and stockholders' equity	$ 55,431	$ 74,939

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

OCULAR THERAPEUTIX, INC.

STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(In thousands, except share and per share data)

	Year Ended December 31,		
	2017	2016	2015
Revenue:			
Product revenue	$ 1,923	$ 1,845	$ 1,354
Collaboration revenue	—	42	396
Total revenue	1,923	1,887	1,750
Costs and operating expenses:			
Cost of product revenue	457	443	319
Research and development	30,880	27,065	26,611
Selling and marketing	17,000	6,701	3,852
General and administrative	15,509	11,004	9,165
Total costs and operating expenses	63,846	45,213	39,947
Loss from operations	(61,923)	(43,326)	(38,197)
Other income (expense):			
Interest income	424	304	166
Interest expense	(1,892)	(1,680)	(1,724)
Other income (expense), net	5	(1)	7
Total other expense, net	(1,463)	(1,377)	(1,551)
Net loss	$ (63,386)	$ (44,703)	$ (39,748)
Net loss per share, basic and diluted	$ (2.20)	$ (1.80)	$ (1.71)
Weighted average common shares outstanding, basic and diluted	28,818,196	24,816,348	23,244,162
Comprehensive loss:			
Net loss	$ (63,386)	$ (44,703)	$ (39,748)
Other comprehensive income (loss):			
Unrealized (loss) gain on marketable securities	5	63	(68)
Total other comprehensive (loss) income	5	63	(68)
Total comprehensive loss	$ (63,381)	$ (44,640)	$ (39,816)

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

OCULAR THERAPEUTIX, INC.

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				
Balances at December 31, 2014	—	$ —	21,333,507	$ 2	$148,122	$ (89,428)	$ —	$ 58,696
Issuance of common stock upon exercise of stock options	—	—	141,848	—	207	—	—	207
Issuance of common stock in connection with employee stock purchase plan	—	—	20,916	—	249	—	—	249
Issuance of common stock upon cashless exercise of warrants	—	—	54,010	—	—	—	—	—
Issuance of common stock upon public offering, net of issuance costs	—	—	3,200,000	—	65,612	—	—	65,612
Unrealized loss on marketable securities	—	—	—	—	—	—	(68)	(68)
Stock-based compensation expense	—	—	—	—	4,640	—	—	4,640
Net loss	—	—	—	—	—	(39,748)	—	(39,748)
Balances at December 31, 2015	—	—	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 gain on marketable securities	—	—	—	—	—	—	63	63
Stock-based compensation expense	—	—	—	—	5,956	—	—	5,956
Net loss	—	—	—	—	—	(44,703)	—	(44,703)
Balances at December 31, 2016	—	—	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)
Balances at December 31, 2017	—	$ —	29,658,202	$ 3	$263,409	$ (237,265)	$ —	$ 26,147

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

OCULAR THERAPEUTIX, INC.

STATEMENTS OF CASH FLOWS

(In thousands)

	Year Ended December 31,		
	2017	**2016**	**2015**
Cash flows from operating activities:			
Net loss	$ (63,386)	$ (44,703)	$ (39,748)
Adjustments to reconcile net loss to net cash used in operating activities			
Stock-based compensation expense	7,321	5,956	4,640
Non-cash interest expense	408	371	166
Depreciation and amortization expense	1,625	881	754
(Gain)/loss on disposal of property and equipment	(5)	1,269	(3)
Purchase of premium on marketable securities	(3)	(37)	(338)
Amortization of premium on marketable securities	17	186	283
Changes in operating assets and liabilities:			
Accounts receivable	24	(57)	136
Prepaid expenses and other current assets	45	924	(53)
Inventory	(9)	21	(1)
Accounts payable	932	(159)	348
Accrued expenses and deferred rent	2,558	1,389	219
Deferred revenue	—	(42)	(146)
Net cash used in operating activities	(50,473)	(34,001)	(33,743)
Cash flows from investing activities:			
Purchases of property and equipment	(8,252)	(1,919)	(1,778)
Proceeds from sale of property and equipment	5	2	7
Change in restricted cash	114	(1,500)	60
Purchases of marketable securities	(3,000)	(41,699)	(91,684)
Proceeds from maturities of marketable securities	38,200	80,684	54,826
Net cash provided by (used in) investing activities	27,067	35,568	(38,569)
Cash flows from financing activities:			
Proceeds from issuance of notes payable	3,700	—	1,897
Proceeds from exercise of stock options	685	199	207
Proceeds from issuance of common stock pursuant to employee stock purchase plan	276	278	249
Proceeds from issuance of common stock offering, net	29,238	627	65,612
Payments of insurance costs financed by a third party	(591)	(519)	(762)
Repayment of notes payable	(1,300)	—	(1,500)
Net cash provided by financing activities	32,008	585	65,703
Net increase in cash and cash equivalents	8,602	2,152	(6,609)
Cash and cash equivalents at beginning of period	32,936	30,784	37,393
Cash and cash equivalents at end of period	$ 41,538	$ 32,936	$ 30,784
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 1,461	$ 1,301	$ 1,251
Supplemental disclosure of non-cash investing and financing activities:			
Additions to property and equipment included in accounts payable at balance sheet dates	$ 538	$ 451	$ 293
Insurance premium financed by a third party	$ —	$ 722	$ 706
Public offering costs included in accounts payable and accrued expenses at balance sheet dates	$ 108	$ —	$ —

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

OCULAR THERAPEUTIX, INC.

NOTES TO 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 bioresorbable hydrogel-based product candidates are designed to tailor duration and amount of delivery of a range of therapeutic agents of varying duration in its product candidates. 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 product 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, 2017, the Company's lead product candidates were 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, subject to submitting its new drug application, or NDA, for post-surgical ocular pain and receiving FDA approval.

Under Accounting Standards Update, or ASU, 2014-15, Presentation of Financial Statements—Going Concern (Subtopic 205-40) ("ASC 205-40"), the Company has the responsibility to evaluate whether conditions and/or events raise substantial doubt about its ability to meet its future financial obligations as they become due within one year after the date that the financial statements are issued. As required by ASC 205-40, this evaluation shall initially not take into consideration the potential mitigating effects of plans that have not been fully implemented as of the date the financial statements are issued. Management has assessed the Company's ability to continue as a going concern in accordance with the requirement of ASC 205-40.

The Company believes that its existing cash and cash equivalents, which includes the $35,100 in net proceeds obtained in the January 2018 public offering of the Company's common stock (Note 19), will enable it to fund its operating expenses, debt service obligations and capital expenditure requirements through the first quarter of calendar year 2019. Management has determined that the Company's accumulated deficit, history of losses, negative cash flows from operations and future expected losses meet the ASC 205-40 standard for raising substantial doubt about the Company's ability to continue as a going concern within one year of the issuance date of these 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, 2017, the Company had an accumulated deficit of $237,265.

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. As such, under the requirements of ASC 205-40, management may

not consider the potential for future capital raises in their assessment of the Company's ability to meet its obligations for the next twelve months.

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. As such, under the requirements of ASC 205-40, the full extent to which management may extend the Company's funds through these actions may not be considered in management's assessment of the Company's ability to continue as a going concern for the next twelve months as defined by ASC 205-40.

Therefore, in accordance with the requirements of ASC 205-40, management has concluded that it is required to disclose that substantial doubt exists about the Company's ability to continue as a going concern for one year from the date these financial statements are issued.

The accompanying 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

Use of Estimates

The preparation of 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 financial statements, and the reported amounts of revenues and expenses during the reporting periods. Significant estimates and assumptions reflected in these 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

The Company recognizes revenue when the following four criteria are met in accordance with Accounting Standards Codification ("ASC") 605, *Revenue Recognition*: persuasive evidence of a sales arrangement exists; delivery of goods has occurred through transfer of title and risk and rewards of ownership; the selling price is fixed or determinable; and collectability is reasonably assured.

The Company records revenue from product sales net of applicable provisions for returns, chargebacks, discounts, wholesaler management fees, government and commercial rebates, and other applicable allowances in the same period in which the related sales are recorded, based on the underlying contract terms.

The Company analyzes multiple-element arrangements based on the guidance in ASC Topic 605-25, *Revenue Recognition—Multiple-Element Arrangements* ("ASC 605-25"). Pursuant to this guidance, the Company evaluates multiple-element arrangements to determine (1) the deliverables included in the arrangement and (2) whether the individual deliverables represent separate units of accounting or whether they must be accounted for as a combined unit of accounting. This evaluation involves subjective determinations and requires management to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that: the delivered item has value to the customer on a standalone basis and, if the arrangement includes a general right of return relative to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in the control of the Company.

In assessing whether an item has standalone value, the Company considers factors such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can use the other deliverables for their intended purpose without the receipt of the remaining elements, whether the value of the deliverable is dependent on the undelivered items and whether there are other vendors that can provide the undelivered elements.

Arrangement consideration that is fixed or determinable is allocated among the separate units of accounting using the relative selling price method. Then, the applicable revenue recognition criteria in ASC 605 are applied to each of the separate units of accounting in determining the appropriate period and pattern of recognition. The Company determines the selling price of a unit of accounting following the hierarchy of evidence prescribed by ASC 605-25. Accordingly, the Company determines the estimated selling price for units of accounting within each arrangement using vendor-specific objective evidence ("VSOE") of selling price, if available; third-party evidence ("TPE") of selling price, if VSOE is not available; or best estimate of selling price ("BESP"), if neither VSOE nor TPE is available. The Company typically uses BESP to estimate the selling price as it generally does not have VSOE or TPE of selling price for its units of accounting. Determining the BESP for a unit of accounting requires significant judgment. In developing the BESP for a unit of accounting, the Company considers applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. The Company validates the BESP for units of accounting by evaluating whether changes in the key assumptions used to determine the BESP will have a significant effect on the allocation of arrangement consideration between multiple units of accounting.

The Company recognizes arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria in ASC 605 are satisfied for that particular unit of accounting. The Company will recognize as revenue arrangement consideration attributed to licenses that have standalone value relative to the other deliverables to be provided in an arrangement upon delivery. The Company will recognize as revenue arrangement consideration attributed to licenses that do not have standalone value relative to the other deliverables to be provided in an arrangement over the Company's estimated performance period, as the arrangement would be accounted for as a single unit of accounting.

At the inception of an arrangement that includes milestone payments, the Company evaluates whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether: (i) the consideration is commensurate with either the Company's performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the Company's performance to achieve the milestone, (ii) the consideration relates solely to past performance, and (iii) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. The Company evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the respective milestone and the level of effort and investment required to achieve the respective milestone in making this assessment. There is considerable judgment involved in determining whether a milestone satisfies all of the criteria required to conclude that a milestone is substantive. Accordingly, pursuant to the guidance of ASC Topic 605-28, *Revenue Recognition—Milestone Method* ("ASC 605-28"), revenue from milestone payments will be recognized in its entirety upon successful accomplishment of the milestone, assuming all other revenue recognition criteria are met.

Other contingent, event-based payments received for which payment is either contingent solely upon the passage of time or the results of a collaborative partner's performance would not be considered milestones under ASC 605-28. In accordance with ASC 605-25, such payments will be recognized as revenue when all of the four basic revenue recognition criteria are met.

Whenever the Company determines that an element is delivered over a period of time, revenue is recognized using either a proportional performance model or a straight-line model over the period of performance. At each reporting period, the Company reassesses its cumulative measure of performance and makes appropriate adjustments, if necessary. The Company recognizes revenue using the proportional performance model whenever the Company can make reasonably reliable estimates of the level of effort required to complete its performance obligations under an arrangement. Revenue recognized under the proportional performance model at each reporting period is determined by multiplying the total expected payments under the contract (excluding payments contingent upon achievement of milestones) by the ratio of the level of effort incurred to date to the estimated total level of effort required to complete the performance obligations under the arrangement. Revenue is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the proportional performance model as of each reporting period. Alternatively, if the Company cannot make reasonably reliable estimates the level of

effort required to complete its performance obligations under an arrangement, then revenue under the arrangement is recognized on a straight-line basis over the period expected to complete the Company's performance obligations. If and when a contingent milestone payment is earned, the additional consideration to be received is added to the total expected payments under the contract. Revenue is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined on a straight-line basis as of the period end date. If the Company cannot reasonably estimate when its performance obligation period ends, then revenue is deferred until the Company can reasonably estimate when the performance obligation period ends.

Inventory Valuation

Inventory is valued at the lower of cost or market, 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:

	December 31,	
	2017	2016
Raw materials	$ 68	$ 58
Work-in-process	37	40
Finished goods	17	15
	$ 122	$ 113

Restricted Cash

As of December 31, 2017 and 2016, the Company held certificates of deposit of $1,614 and $1,728, respectively, as security deposits for the lease of the Company's manufacturing space and current corporate headquarters (Note 13). The Company has classified this as long-term restricted cash on its balance sheet.

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 and marketable securities. The Company has all cash and cash equivalents and marketable securities 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 and marketable securities 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, 2017 and 2016, the carrying value of the Company's outstanding notes payable (Note 7) approximates fair value based on the interest rate for the borrowings outstanding.

Marketable Securities

The Company's marketable securities are classified as available-for-sale and are carried at fair value with the unrealized gains and losses reported as a component of accumulated other comprehensive income (loss) in stockholders' equity. Realized gains and losses and declines in value judged to be other than temporary are included as a component of other income (expense), net based on the specific identification method. Fair value is determined based on quoted market prices.

At December 31, 2017, the Company does not have marketable securities.

At December 31, 2016, marketable securities by security type consisted of:

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
United States treasury notes	$ 35,216	$ 1	$ (8)	$ 35,209
Total	$ 35,216	$ 1	$ (8)	$ 35,209

At December 31, 2016, marketable securities consisted of investments that mature within one year.

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.

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 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 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. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

The Company accounts for uncertainty in income taxes recognized in the 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 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-based product candidates for the sustained 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 (deficit) that result from transactions and economic events other than those with stockholders. For the years ended December 31, 2017, 2016 and 2015, other comprehensive loss consisted of unrealized gains (losses) from marketable securities.

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 and warrants for the purchase of Redeemable Preferred Stock. 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, 2017, 2016 and 2015.

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 statement of operations. Deferred offering costs amounted to $108 at December 31, 2017 and are capitalized in prepaid expenses and other current assets. There were no deferred offering costs at December 31, 2016.

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 financial statements.

Recently Issued Accounting Pronouncements

In May 2014, the FASB issued ASU No. 2014-09, Revenue from Contracts with Customers (Topic 606) ("ASU 2014-09"). ASU 2014-09 outlines a new, single comprehensive model for entities to use in accounting for revenue arising from contracts with customers and supersedes most current revenue recognition guidance, including industry-specific guidance. This new revenue recognition model provides a five-step analysis in determining when and how revenue is recognized. The new model will require revenue recognition to depict the transfer of promised goods or services to customers in an amount that reflects the consideration a company expects to receive in exchange for those goods or services. In August 2015, the FASB issued ASU No. 2015-14, Revenue from Contracts with Customers (Topic 606): Deferral of Effective Date which delays the effective date of ASU 2014-09 such that the standard is effective for public entities for annual periods beginning after December 15, 2017 and for interim periods within those fiscal years. The FASB subsequently issued amendments to ASU No. 2014-09 that have the same effective date and transition date, all of which collectively are herein referred to as "the New Revenue Standard."

The New Revenue Standard became effective for the Company on January 1, 2018 and will be adopted using the modified retrospective method. The Company has performed a review of the New Revenue Standard as compared to its current accounting policies and determined that the adoption of the New Revenue Standard will not have a material impact on its financial statements and footnote disclosures.

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 as a right –of-use asset and a lease liability. Leases will be classified as either operating or financing and classification will be based on criteria similar to current lease accounting but without bright lines. The guidance is effective for annual reporting periods beginning after December 15, 2018 and interim period within those fiscal years and early adoption is permitted. The Company is currently assessing the impact that the adoption of ASU 2016-02 will have on its financial statements and footnote disclosures.

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 guidance in ASU 2016-15 is required for annual reporting periods beginning after December 15, 2017, including interim periods within those fiscal years. The Company adopted ASU 2016-15 as of the required effective date of January 1. 2018 and does not expect the adoption will have a material impact on its 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 will adopt ASU 2016-18 as of the required effective date of January 1, 2018 and will reflect the adoption retrospectively to all periods presented. Upon adoption, the Company's statements of cash flows will include restricted cash with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on such statements. The Company has restricted cash of $1,614 at December 31, 2017.

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 will adopt ASU 2017-09 as of the required effective date of January 1, 2018. The adoption of ASU 2017-09 will have an impact on the accounting for the modification of stock-based awards, if any, after the date of the adoption.

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, 2017 and 2016 and indicate the level of the fair value hierarchy utilized to determine such fair value:

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

	Fair Value Measurements as of December 31, 2016 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ —	$ 20,734	$ —	$ 20,734
Agency bonds	—	8,994	—	8,994
Marketable securities:				
United States treasury notes	—	35,209	—	35,209
Total	$ —	$ 64,937	$ —	$ 64,937

During the years ended December 31, 2017, 2016 and 2015, 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,	
	2017	2016
Equipment	$ 6,183	$ 4,361
Leasehold improvements	8,553	906
Furniture and fixtures	740	418
Software	118	89
Construction in progress	225	1,357
	15,819	7,131
Less: Accumulated depreciation	(5,341)	(3,818)
	$ 10,478	$ 3,313

Depreciation expense was $1,625, $881 and $754 for the years ended December 31, 2017, 2016 and 2015, respectively.

At December 31, 2016, the remaining construction in progress was related to the build-out of the Company's new facility and equipment that is being used in that facility.

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, 2017	December 31, 2016
Accrued payroll and related expenses	$ 2,936	$ 2,146
Accrued rent	267	—
Accrued professional fees	534	1,018
Accrued research and development expenses	217	360
Accrued insurance	—	591
Accrued other	356	520
	$ 4,310	$ 4,635

6. Collaboration and Feasibility Agreements

The Company had entered into a feasibility agreement with a biotechnology company in October 2014. Under this agreement, the biotechnology company would pay up to $700, of which $250 was a non-refundable payment due upon contract execution and $450 will be due upon the achievement of certain milestones. The Company recognized the total expected payments under the contract which included only the non-refundable payments on a straight-line basis over the estimated performance period. When a contingent milestone payment was earned, the additional consideration to be received was added to the total expected payments under the contract then recognized over the estimated performance period. In January 2015, the first milestone under the feasibility agreement was achieved triggering a non-refundable payment due of $250 such that the total non-refundable payments that were recognized over the estimated performance period totaled $500. This agreement was terminated in the second quarter of 2016 and the Company does not have any further obligations. The Company recognized revenue of $0, $42 and $396 for the years ended December 31, 2017, 2016 and 2015, respectively. As of December 31, 2017 and 2016, the Company had no deferred revenue and no accounts receivable related to this agreement.

On October 10, 2016, the Company entered into a Collaboration, Option and License Agreement (the "Collaboration Agreement") with Regeneron Pharmaceuticals, Inc. ("Regeneron") for the development and potential commercialization of products using the Company's hydrogel in combination with Regeneron's large molecule VEGF-targeting compounds for the treatment of retinal diseases. The Collaboration Agreement does not cover the development of any 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. 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 had a total borrowing capacity of $15,000 which has been fully drawn down. In connection with the Company’s entry into the 2014 Credit Facility a previously outstanding credit agreement issued in 2011 (the “2011 Credit Facility”) was terminated.

The Company was obligated to make monthly, interest-only payments until September 30, 2015 and, thereafter, to pay 30 consecutive, equal monthly installments of principal from October 1, 2015 through March 1, 2018 plus interest. The loan under the 2014 Credit Facility bears interest at an annual rate of 8.25%. In addition, a final payment equal to 3.75% of amounts drawn under the 2014 Credit Facility was due upon its maturity date. This amount was being accreted to the carrying value of the debt, using the effective interest method. In connection with the draw-down in 2014, the lenders received warrants to purchase 100,000 shares of the Company’s Series D-1 redeemable convertible preferred stock with an exercise price of $3.00 per share, which are exercisable until April 2021. The fair value of the warrants as of the issuance date totaling $326 was recorded as a preferred stock warrant liability. Of this amount, $290 was allocated to the 2014 Credit Facility and recorded as debt discount and $36 was allocated to the 2011 Credit Facility and recorded as loss on extinguishment of debt (see below). The effective annual interest rate of the outstanding debt under the 2014 Credit Facility was 11%.

In December 2015, the 2014 Credit Facility was amended (the “Amended Credit Facility”) to increase the aggregate principal amount to $15,600 and extend both the interest-only payment period and the maturity date. At the time of the amendment, the Company had $13,500 in outstanding principal. Net proceeds from the Amended Credit Facility were $1,897. The Company was obligated to make monthly interest-only payments under the Amended 2014 Credit Facility until December 31, 2016 and, thereafter, was required to make monthly payments of principal and interest from January 1, 2017 through December 1, 2019. The interest rate under the Amended Credit Facility was unchanged at an annual rate of 8.25%. In addition, a final payment equal to 3.75% of amounts drawn under the Amended Credit Facility is due upon the new maturity date. There are no financial covenants associated with the Amended Credit Facility and the negative covenants remain unchanged. The Company accounted for the amendment of the 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 10.6%.

In March 2017, the Company further 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. Given the debt was refinanced prior to the issuance of the 2016 financial statements, the Company classified the debt balance at December 31, 2016, with the exception of payments made prior to the refinancing, as long-term in accordance with the terms of the 2017 Amended Credit Facility.

The Company was obligated to make interest-only payments under the 2017 Amended Credit Facility until February 1, 2018. Thereafter, it is required to make monthly principal and interest payments through December 1, 2020. Amounts borrowed under the Amended Credit Facility are 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 is due upon the maturity date of December 1, 2020.

There are no financial covenants associated with the 2017 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 obligations under the 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 personal property, other than its intellectual property.

The Company accounted for the 2017 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 10.5%.

As of December 31, 2017, the annual repayment requirements for the 2017 Amended Credit Facility, inclusive of the final payment of $630 due at expiration, were as follows:

Year Ending December 31,	Principal	Interest and Final Payment	Total
2018	$ 5,658	$ 1,308	$ 6,966
2019	6,171	796	6,967
2020	6,171	911	7,082
	$ 18,000	$ 3,015	$ 21,015

8. Warrants

The Company has warrants for the purchase of 18,939 shares of common stock remain outstanding at December 31, 2017 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, 2017.

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 June 2015, the Company completed a follow-on offering of its 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 the Company and 1,400,000 shares were sold by certain stockholders of the Company, including those shares sold in connection with the exercise by the underwriters of their option to purchase additional shares. The Company received net proceeds from the follow-on offering of $65,612 after deducting underwriting discounts and offering expenses.

In November 2016, the Company entered into an at-the-Market sales agreement, (the "2016 ATM 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 ATM Agreement resulting in net proceeds of approximately $626 after underwriting discounts, commission and other offering expenses. In January 2017, the Company sold 161,341 shares of common stock under the 2016 ATM Agreement, resulting in net proceeds of approximately $1,395 after

underwriting discounts and commissions. In March 2017, the Company sold 177,068 shares of common stock under the 2016 ATM Agreement, resulting in net proceeds of approximately $1,561 after underwriting discounts, commissions and expenses. In April 2017, the Company sold 93,730 shares of common stock under the 2016 ATM Agreement, resulting in net proceeds of approximately $855 after underwriting discounts and commissions. In September 2017, the Company sold 258,860 shares of common stock under the 2016 ATM Agreement, resulting in net proceeds of approximately $1,573 after underwriting discounts and commissions. In October 2017, the Company sold 97,492 shares of common stock under the 2016 ATM Agreement, resulting in net proceeds of approximately $593 after underwriting discounts and commissions.

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.

As of December 31, 2017, the Company had reserved 6,161,620 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, 2017, the number of shares available for issuance under the 2014 Plan increased by 1,000,964. As of December 31, 2017, 1,805,633 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, 2017, the number of shares available for issuance under the 2014 Plan increased by 125,121. As of December 31, 2017, 334,674 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, 2017, there were outstanding unvested service-based stock options held by nonemployees for the purchase of 474 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,		
	2017	2016	2015
Risk-free interest rate	2.00 %	1.42 %	1.67 %
Expected term (in years)	6	6	6
Expected volatility	102 %	85 %	71 %
Expected dividend yield	— %	— %	— %

The following table summarizes the Company's stock option activity:

	Shares Issuable Under Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (In years)	Aggregate Intrinsic Value
Outstanding as of December 31, 2016	3,091,480	$ 10.77	7.3	$ 6,659
Granted	2,354,150	8.01		
Exercised	(220,520)	3.11		
Forfeited	(1,222,736)	9.12		
Outstanding as of December 31, 2017	4,002,374	$ 10.08	7.2	$ 1,222
Options vested and expected to vest as of December 31, 2017	3,885,480	$ 10.12	7.2	$ 1,222
Options exercisable as of December 31, 2017	1,970,539	$ 9.34	9.0	$ 2

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 $408, $575 and $3,192 during the years ended December 31, 2017, 2016 and 2015, respectively.

The weighted average grant date fair value of stock options granted to employees and directors during the years ended December 31, 2017, 2016, 2015 was $6.44, $4.52 and $18.12 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. The aggregate intrinsic value of restricted stock awards that vested during the years ended December 31, 2017, 2016 and 2015 was $0, $0, and $265, respectively. There were no remaining restricted shares at December 31, 2017 and 2016.

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:

	Year Ended December 31,		
	2017	2016	2015
Research and development	$ 2,584	$ 1,900	$ 1,589
Selling and marketing	633	490	340
General and administrative	4,104	3,566	2,711
	$ 7,321	$ 5,956	$ 4,640

As of December 31, 2017, the Company had an aggregate of $11,874 of unrecognized stock-based compensation cost, which is expected to be recognized over a weighted average period of 2.8 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, 2017, 2016 and 2015:

	Year Ended December 31,		
	2017	2016	2015
Numerator:			
Net loss attributable to common stockholders	$ (63,386)	$ (44,703)	$ (39,748)
Denominator:			
Weighted average common shares outstanding, basic and diluted	28,818,196	24,816,348	23,244,162
Net loss per share attributable to common stockholders, basic and diluted	$ (2.20)	$ (1.80)	$ (1.71)

The Company excluded the following common stock equivalents, outstanding as of December 31, 2017, 2016, and 2015, from the computation of diluted net loss per share attributable to common stockholders for the years ended December 31, 2017, 2016 and 2015 because they had an anti-dilutive impact due to the net loss incurred for the periods.

	December 31,		
	2017	2016	2015
Options to purchase common stock	4,002,374	3,091,480	2,115,519
Warrants for the purchase of common stock	18,939	18,939	18,939
	4,021,313	3,110,419	2,134,458

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, 2017 are as follows:

Year Ending December 31,	
2018	1,715
2019	1,808
2020	1,850
2021	1,886
2022	1,936
Thereafter	6,954
Total	$ 16,149

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, shall be $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 must be used on or before December 31, 2017, or it will 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. 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, 2017, 2016 and 2015, the Company recognized $1,733, $1,084 and $778, 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, 2017, royalties paid under this agreement related to product sales were $154.

On February 12, 2014, the Company issued to Incept 189,393 shares of its common stock in connection with the expansion of the scope of the license to include back-of-the-eye technology held by Incept (Note 16).

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 financial statements as of December 31, 2017.

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, 2017, 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 have been 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). Motions to consolidate these three actions and appoint lead plaintiff(s) for the consolidated action are currently pending.

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 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. Sawney 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 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, 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 the same defendants and is premised on substantially similar allegations as the previous *Corwin* and *Madera* complaints, and asserts claims for breach of fiduciary duty against the individual defendants and unjust enrichment against the two SV entity defendants. The response to the consolidated complaint is due on April 17, 2018.

On January 31, 2018, a third purported shareholder derivative suit was filed against certain of the Company 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, but does not name either SV Life Sciences Fund, IV, LP or SV Life Sciences Fund IV Strategy Partners, LP as a defendant. The complaint purports to assert derivative claims against the individual defendants for breach of fiduciary duty 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 seeks declaratory, equitable and monetary relief, an unspecified amount of damages, with interest, and attorneys' fees and costs.

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.

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 FDA, investors and others. 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.

The Company is still in the process of analyzing the impact to the Company of the TCJA. Where the Company has been able to make reasonable estimates of the effects the Company has recorded provisional amounts. The ultimate impact to the Company's financial statements of the TCJA may differ from the provisional amounts due to, among other things, additional analysis, changes in interpretations and assumptions the Company has made, additional regulatory guidance that may be issued, and actions the Company may take as a result of the TCJA. The accounting is expected to be complete when the Company's 2017 U.S. corporate income tax return is filed in 2018.

Income Taxes

During the years ended December 31, 2017, 2016 and 2015, the Company recorded no income tax benefits for the net operating losses incurred or the research and development tax credits generated in each year, due to its uncertainty of realizing a benefit from those items.

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,		
	2017	2016	2015
Federal statutory income tax rate	(34.0)%	(34.0)%	(34.0)%
Tax reform change	43.0	—	—
Research and development tax credits	(3.3)	(2.9)	(3.1)
State taxes, net of federal benefit	(3.8)	(4.8)	(2.0)
Stock-based compensation	2.2	1.4	1.2
Other	(0.2)	(0.6)	(0.2)
Change in deferred tax asset valuation allowance	(3.9)	40.9	38.1
Effective income tax rate	— %	— %	— %

Net deferred tax assets consisted of the following:

	December 31,	
	2017	2016
Net operating loss carryforwards	$ 33,094	$ 31,960
Tax credit carryforwards	7,971	5,482
Capitalized start-up costs	1,022	1,723
Capitalized research and development expenses, net	21,869	26,943
Accrued expenses and other temporary differences	3,770	4,128
Total gross deferred tax assets	67,726	70,236
Valuation allowance	(67,726)	(70,236)
Net deferred tax assets	$ —	$ —

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2017, 2016 and 2015 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:

	Year Ended December 31,		
	2017	2016	2015
Valuation allowance as of beginning of year	$ 70,236	$ 51,969	$ 36,825
Increases recorded to income tax provision	24,773	18,267	15,144
Decreases recorded to income tax provision	(27,283)	—	—
Valuation allowance as of end of year	$ 67,726	$ 70,236	$ 51,969

As of December 31, 2017, the Company had net operating loss carryforwards for federal and state income tax purposes of $126,229 and $109,258, respectively, which begin to expire in 2026 and 2026, respectively. As of December 31, 2017, the Company also had available research and development tax credit carryforwards for federal and state income tax purposes of $5,518 and $2,813, 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, 2017 and 2016. The valuation allowance, on a net basis, decreased by approximately $2,510 in 2017 primarily as a result of the decrease in the corporate tax rate offset by increase in deferred tax assets primarily related to net operating loss carryforwards.

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2017 or 2016.

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,

2014 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, 2017 and 2016, 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, 2017, 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.

During the years ended December 31, 2017, 2016 and 2015, the Company invoiced Augmenix, Inc. ("Augmenix") $0, $0 and $4, respectively, for consulting and other services. During the years ended December 31, 2017, 2016 and 2015, Augmenix invoiced the Company $0, $0 and $0 for legal fees paid by Augmenix on behalf of the Company. Certain shareholders of Augmenix are holders of the Company's common stock. In addition, certain employees of the Company are shareholders of Augmenix. The Company's Executive Chairman was also the Chief Executive Officer of Augmenix up until April 2014 and is currently the Chairman of the board of directors of Augmenix.

In April 2014, the Company granted 28,437 shares of restricted common stock to its Executive Chairman of the Board of Directors, who was serving as the Company's Chief Executive Officer, in lieu of $250 of such officer's 2015 base salary. During 2015, due to an administrative error, the Company did not appropriately adjust the base salary to reflect this reduction. As a result, the Company paid the full base salary for 2015. Upon discovery of the error, the officer promptly repaid the full $250 to the Company on April 1, 2016. The Company recorded a reduction to payroll expense in the first quarter of 2016. The effect of this error on the statement of operations was considered immaterial for all related periods.

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 and 2016, 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 and 2016, there was $194 and $0, respectively, recorded in accounts payable for WilmerHale. As of December 31, 2017 and 2016, there was $80 and $20, respectively, 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 marking, 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:

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

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

	Twelve Months Ended December 31, 2017
Restructuring and other costs reserve beginning balance	$ —
Restructuring and other costs expenses incurred during the period	2,506
Amounts paid during the period	(1,546)
Restructuring and other costs reserve ending balance	$ 960

18. Selected Quarterly Financial Data (Unaudited)

	Three Months Ended							
	Dec. 31, 2017	Sept. 30, 2017	June 30, 2017	Mar 31, 2017	Dec. 31, 2016	Sept. 30, 2016	June 30, 2016	Mar 31, 2016
Statements of Operations Data:								
Product revenue	$ 487	$ 523	$ 438	$ 475	$ 511	$ 477	$ 441	$ 416
Collaboration revenue	—	—	—	—	—	—	—	42
Revenue	487	523	438	475	511	477	441	458
Loss from operations	(12,716)	(15,196)	(18,339)	(15,672)	(12,472)	(9,238)	(11,107)	(10,509)
Net loss	(13,102)	(15,567)	(18,694)	(16,023)	(12,822)	(9,596)	(11,445)	(10,840)
Basic and diluted net loss per common share	$ (0.44)	$ (0.54)	$ (0.64)	$ (0.58)	$ (0.52)	$ (0.39)	$ (0.46)	$ (0.44)

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, 2018, the number of shares available for issuance under the 2014 Plan increased by 1,186,328.

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 ESPP increased by 148,291.

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 $35,100 after deducting underwriting discounts, commissions and expenses.

EMPLOYMENT AGREEMENT

This EMPLOYMENT AGREEMENT (the "Agreement") is made as of July 31, 2017 (the "Effective Date"), by and between Ocular Therapeutix, Inc., a Delaware corporation (the "Company"), and Daniel Bollag ("Executive"). In consideration of the mutual covenants contained in this Agreement, the Company and Executive agree as follows:

1. Employment. The Company agrees to employ Executive and Executive agrees to be employed by the Company on the terms and conditions set forth in this Agreement.

(a) Capacity. Executive shall serve the Company as Sr. Vice President, Regulatory Affairs, Pharmacovigilance and Quality reporting to the Company's Chief Executive Officer (the "CEO"). During the Term (as defined below) of Executive's employment with the Company, Executive shall, subject to the direction of the CEO, have the responsibilities, duties and authority commensurate with the position of Sr. Vice President, Regulatory Affairs, Pharmacovigilance and Quality and shall perform such other duties as may from time to time be reasonably assigned to him by the Company. The Company may change Executive's position, duties, and work location as it deems necessary.

(b) Devotion of Duties; Representations. During the Term of Executive's employment with the Company, Executive shall devote 100% of his reasonable best efforts and full business time and energies to the business and affairs of the Company, and shall endeavor to perform the duties and services contemplated hereunder to the reasonable satisfaction of the Company. During the Term of Executive's employment with the Company, Executive shall not, without the prior written approval of the Company (by action of the Company's Board of Directors (the "Board"), undertake any other employment from any person or entity or serve as a director of any other company; provided, however, that (i) the Company will entertain requests as to such other employment or directorships in good faith and (ii) Executive will be eligible to participate in any policy relating to outside activities that is applicable to the senior executives of the Company and approved by the Board after the date hereof, and provided further that in no event may any such business activity be undertaken if it would (x) be in violation of any provision of this Agreement or other agreement between Executive and the Company, (y) interfere with the performance of Executive's duties for the Company, or (z) present a conflict of interest with the Company's business interests.

2. Term of Employment.

(a) Executive's employment hereunder shall be at-will and begin on the Effective Date. Executive's employment hereunder shall be terminated upon the first to occur of the following:

(i) Immediately upon Executive's death;

(ii) By the Company, by written notice to Executive effective as of the date of such notice (or on such other date as specified in such notice):

(A) Following the Disability of Executive. "Disability" means that Executive (i) is unable to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment which can be

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

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

(C) Subject to Section 4 hereof, without Cause;

(iii) By Executive:

(A) At any time by written notice to the Company, effective thirty (30) days after the date of such notice; or

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

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

(b) Definition of "Cause". For purposes of this Agreement, "Cause" shall, pursuant to the reasonable good faith determination by the Company as documented in writing, include: (i) the willful and continued failure by Executive to substantially perform Executive's material duties or responsibilities under this Agreement (other than such a failure as a result of Disability); (ii) any action or omission by Executive involving willful misconduct or gross negligence with regard to the Company, which has a detrimental effect on the Company; (iii) Executive's conviction of a felony, either in connection with the performance of Executive's obligations to the Company or which otherwise shall adversely affect Executive's ability to perform such obligations or shall materially adversely affect the business activities, reputation, goodwill or image of the Company; (iv) the material breach by Executive of a fiduciary duty to the Company; or (v) the material breach by Executive of any of the provisions of this Agreement, provided that any breach of Executive's obligations with respect to Sections 5 or 6 of this Agreement, subject to the cure provision in the next sentence, shall be deemed "material." In respect of the events described in clauses (i) and (v) above, the Company shall give Executive notice of the failure of performance or breach, reasonable as to time, place and manner in the circumstances, and a 30-day opportunity to cure, provided that such failure of performance or breach is reasonably amenable to cure as determined by the Company in its sole discretion.

(c) Definition of "Good Reason". For purposes of this Agreement, a "Good Reason" shall mean any of the following, unless (i) the basis for such Good Reason is cured within a reasonable period of time (determined in the light of the cure appropriate to the basis of such Good Reason, but in no event less than thirty (30) nor more than ninety (90) days) after the Company receives written notice (which must be received from Executive within ninety (90) days of the initial existence of the condition giving rise to such Good Reason) specifying the basis for such Good Reason or (ii) Executive has consented to the condition that would otherwise be a basis for Good Reason:

(i) A change in the principal location at which Executive provides services to the Company to a location more than fifty (50) miles from such principal location (which change, the Company has reasonably determined as of the date hereof, would constitute a material change in the geographic location at which Executive provides services to the Company), provided that such a relocation shall not be deemed to occur under circumstances where Executive's responsibilities require him to work at a location other than the corporate headquarters for a reasonable period of time not to exceed sixty (60) consecutive days or such longer period as may be determined by mutual agreement;

(ii) A material adverse change by the Company in Executive's duties, authority or responsibilities which causes Executive's position with the Company to become of materially less responsibility or authority than Executive's position immediately following the Effective Date where such change is not remedied within ten (10) business days after written notice thereof by Executive;

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

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

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

(d) Definition of "Corporate Change". For purposes of this Agreement, "Corporate Change" shall mean any circumstance in which (i) the Company is not the surviving entity in any merger, consolidation or other reorganization (or survives only as a subsidiary or affiliate of an entity other than a previously wholly-owned subsidiary of the Company); (ii) the Company sells, leases or exchanges all or substantially all of its assets to any other person or entity (other than a wholly-owned subsidiary of the Company); (iii) any person or entity, including a "group" as contemplated by Section 13(d)(3) of the Securities Exchange Act of 1934 (excluding, for this purpose, the Company or any subsidiary, or any employee benefit plan of the Company or any subsidiary, or any "group" in which all or substantially all of its members or its members' affiliates are individuals or entities who are or were beneficial owners of the Company's outstanding shares prior to the initial public offering of the Company's common stock), acquires or gains ownership or control (including, without limitations, powers to vote) of more than 50% of the outstanding shares of the Company's voting stock (based upon voting power); or (v) as a result of or in connection with a contested election of directors, the persons who were directors of the Company before such election shall cease to constitute a majority of the Board of Directors of the Company. Notwithstanding the foregoing, a "Corporate Change"

shall not occur as a result of a merger, consolidation, reorganization or restructuring after which either (1) a majority of the Board of Directors of the controlling entity consists of persons who were directors of the Company prior to the merger, consolidation, reorganization or restructuring or (2) all or substantially all of the individuals or entities who were the beneficial owners of the Company's outstanding shares immediately prior to such merger, consolidation, reorganization or restructuring beneficially own, directly or indirectly, more than 50% of the then-outstanding shares of common stock and the combined voting power of the then-outstanding securities entitled to vote generally in the election of directors, respectively, of the resulting or acquiring corporation in substantially the same proportions as their ownership of the Company's outstanding shares immediately prior to the merger, consolidation, reorganization or restructuring. Notwithstanding the foregoing, for any payments or benefits hereunder (including pursuant to Section 4(b)(iii) hereof) or pursuant to any other agreement between the Company and Executive, in either case that are subject to Section 409A, the Corporate Change must constitute a "change in control event" within the meaning of Treasury Regulation Section 1.409A-3(i)(5)(i).

3. Compensation.

(a) Base Salary. Executive's minimum base salary during the Term shall be at the rate of $335,000 per year. Executive's base salary shall be payable in substantially equal installments in accordance with the Company's payroll practices as in effect from time to time, less any amounts required to be withheld under applicable law. The base salary will be subject to adjustment from time to time in the sole discretion of the Company; provided that, the Company covenants that (A) during the first twelve months of Executive's employment, it shall not reduce Executive's base salary and (B) following such twelve month period, it shall not reduce the base salary below the base salary then in effect immediately prior to the reduction unless (i) Executive consents to such reduction, or (ii) the reduction is in connection with a general reduction of not more than 20% in compensation of senior executives of the Company generally that occurs prior to the effective date of any Corporate Change.

(b) Bonus. In addition to the base salary set forth above, the Company may pay Executive an annual bonus (the "Bonus") as determined by the Board, solely in its discretion (it being understood that Executive's target annual bonus shall be 35% of Executive's base salary in effect for such year, but may be higher or lower in any year in the Board's discretion). The Board's decision to issue a Bonus to Executive in any particular year shall have no effect on the absolute discretion of the Board to grant or not to grant a Bonus in subsequent years. Executive must be an active employee of the Company on December 31 of any calendar year in order to be eligible for and to earn any Bonus for that year. Any Bonus for a particular year shall be paid or provided to Executive in a lump sum no later than March 15th of the calendar year following the calendar year in which the Bonus was earned. For the avoidance of doubt, any Bonus for the [current year] calendar year would be prorated.

(c) Stock Option Grant. Subject to approval by the Board, the Company will grant to Executive an option to purchase 110,000 shares of the Company's common stock (the "Option") with the ability to obtain up to 50,000 additional options in Q1'18 dependent upon company and personal performance. The Option is subject to adjustment for stock splits, combinations or other recapitalizations. The exercise price per share of the Option shall be equal to the last reported sale price per share of the common stock on the NASDAQ stock exchange on the effective date of grant of the Option approved by the Board. The Option shall be issued

pursuant to the Company's 2014 Equity Incentive Plan, as it may be amended from time to time, and will be subject to all of the terms and conditions set forth in such plan and the Stock Option Agreement covering the Option.

(d) Vacation. Executive shall be entitled to take 20 days of paid vacation during each year of the Term to be taken at such time or times as shall be mutually convenient and consistent with his duties and obligations to the Company. The number of vacation days for which Executive is eligible shall accrue at the rate of 1.67 days per month. Vacation is at all times subject to the Company's Time-Off Policy, which the Company may change periodically in its sole discretion.

(e) Fringe Benefits. Executive shall be entitled to participate in any employee benefit plans that the Company makes available to its executives (including, without limitation, group life, disability, medical, dental and other insurance, retirement, pension, profit-sharing and similar plans) (collectively, the "Fringe Benefits"), provided that the Fringe Benefits shall not include any stock option or similar plans relating to the grant of equity securities of the Company. These benefits may be modified or changed from time to time at the sole discretion of the Company. Where a particular benefit is subject to a formal plan (for example, medical or life insurance), eligibility to participate in and receive any particular benefit is governed solely by the applicable plan document, and eligibility to participate in such plan(s) may be dependent upon, among other things, a physical examination.

(f) Reimbursement of Expenses. Executive shall be entitled to reimbursement for all ordinary and reasonable out-of-pocket business expenses that are reasonably incurred by him in furtherance of the Company's business in accordance with reasonable policies adopted from time to time by the Company for senior executives, subject to Section 4(d)(v).

4. Severance Compensation.

(a) In the event of any termination of Executive's employment for any reason, the Company shall pay Executive (or Executive's estate) such portions of Executive's base salary as have accrued prior to such termination and have not yet been paid, together with (i) amounts for accrued unused vacation days (as provided above), (ii) any amounts for expense reimbursement which have been properly incurred or the Company has become obligated to pay prior to termination and have not been paid as of the date of such termination and (iii) the amount of any Bonus previously granted to Executive by the Board but not yet paid, which amount shall not include any pro rata portion of any Bonus which would have been earned if such termination had not occurred (the "Accrued Obligations"). Such Accrued Obligations shall be paid as soon as possible after termination, and in any event in accordance with applicable law.

(b) In the event that Executive's employment hereunder is terminated (i) by Executive for a Good Reason or (ii) by the Company without Cause, the Company shall pay to Executive the Accrued Obligations. In addition, the Company shall pay to Executive the severance benefits set forth below for twelve (12) months, or for eighteen (18) months if such termination occurs during the twelve (12) month period following a Corporate Change (the "Protected Period"), following Executive's termination of employment (as applicable, the "Severance Period"). The receipt of any severance benefits provided in this Section shall be dependent upon Executive's execution and, to the extent applicable, nonrevocation of the

Company's standard form of separation and general release of claims agreement (the "Release"), which Release must be signed and any applicable revocation period with respect thereto must have expired by the sixtieth (60th) day following Executive's termination of employment. The severance benefits shall be paid or commence, as applicable, on the first payroll period following the date the Release becomes effective (the "Payment Date"). Notwithstanding the foregoing, if the 60th day following Executive's termination occurs in the calendar year following the date on which Executive's employment terminates, then the Payment Date shall be no earlier than January 1 of such subsequent calendar year.

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

(ii) Only if Executive's employment is terminated (A) by Executive for a Good Reason or (B) by the Company without Cause, in each case during the Protected Period, the Company shall pay Executive an amount equal to one and one-half times his target annual bonus, described in Section 3(b) hereof, for the year in which the termination of employment occurs, which total amount shall be payable in a lump sum on the Payment Date.

(iii) Only if Executive's employment is terminated (A) by Executive for a Good Reason or (B) by the Company without Cause, in each case during the Protected Period, one hundred percent (100%) of Executive's outstanding unvested equity awards granted under the Company's equity and long-term incentive plan(s) prior to his termination shall vest immediately.

(iv) The Company shall continue to provide Executive and his then-enrolled eligible dependents with group health insurance and shall continue to pay the amount of the premium as in effect on the date of such termination for the Severance Period commencing on the effective date of such termination, subject to applicable law and the terms of the respective policies; provided that the Company's obligation to provide the benefits contemplated herein shall terminate upon Executive's becoming eligible for coverage under the medical benefits program of a subsequent employer. The foregoing shall not be construed to extend any period of continuation coverage (e.g., COBRA) required by Federal law.

(c) In the event that Executive's employment hereunder is terminated (i) by Executive for other than a Good Reason, or (ii) by the Company for Cause, or (iii) as a result of Executive's death or Disability, then the Company will pay to Executive the Accrued Obligations. The Company shall have no obligation to pay Executive (or Executive's estate) any other compensation following such termination except as provided in Section 4(a).

(d) Compliance with Section 409A. Subject to the provisions in this Section 4(d), any severance payments or benefits under this Agreement shall begin only upon the date of Executive's "separation from service" (determined as set forth below) which occurs on or after the date of termination of Executive's employment. The following rules shall apply with respect

to the distribution of the severance payments and benefits, if any, to be provided to Executive under this Agreement:

(i) It is intended that each installment of the severance payments and benefits provided under this Agreement shall be treated as a separate "payment" for purposes of Section 409A. Neither the Company nor Executive shall have the right to accelerate or defer the delivery of any such payments or benefits except to the extent specifically permitted or required by Section 409A.

(ii) If, as of the date of Executive's "separation from service" from the Company, Executive is not a "specified employee" (within the meaning of Section 409A), then each installment of the severance payments and benefits shall be made on the dates and terms set forth in this Agreement.

(iii) If, as of the date of Executive's "separation from service" from the Company, Executive is a "specified employee" (within the meaning of Section 409A), then:

(A) Each installment of the severance payments and benefits due under this Agreement that, in accordance with the dates and terms set forth herein, will in all circumstances, regardless of when the separation from service occurs, be paid within the short-term deferral period (as defined under Section 409A) shall be treated as a short-term deferral within the meaning of Treasury Regulation Section 1.409A-1(b)(4) to the maximum extent permissible under Section 409A and such payments and benefits shall be paid or provided on the dates and terms set forth in this Agreement; and

(B) Each installment of the severance payments and benefits due this Agreement that is not described in Section 4(d)(iii)(A) above and that would, absent this subsection (B), be paid within the six-month period following Executive's "separation from service" from the Company shall not be paid until the date that is six months and one day after such separation from service (or, if earlier, Executive's death), with any such installments that are required to be delayed being accumulated during the six-month period and paid in a lump sum on the date that is six months and one day following Executive's separation from service and any subsequent installments, if any, being paid in accordance with the dates and terms set forth herein; provided, however, that the preceding provisions of this sentence shall not apply to any installment of severance payments and benefits if and to the maximum extent that such installment is deemed to be paid under a separation pay plan that does not provide for a deferral of compensation by reason of the application of Treasury Regulation 1.409A-1(b)(9)(iii) (relating to separation pay upon an involuntary separation from service). Any installments that qualify for the exception under Treasury Regulation Section 1.409A-1(b)(9)(iii) must be paid no later than the last day of Executive's second taxable year following the taxable year in which the separation from service occurs.

(iv) The determination of whether and when Executive's separation from service from the Company has occurred shall be made in a manner consistent with,

and based on the presumptions set forth in, Treasury Regulation Section 1.409A-1(h). Solely for purposes of this Section 4(d)(iv), "Company" shall include all persons with whom the Company would be considered a single employer under Section 414(b) and 414(c) of the Code.

(v) All reimbursements and in-kind benefits provided under this Agreement shall be made or provided in accordance with the requirements of Sections 409A to the extent that such reimbursements or in-kind benefits are subject to Section 409A, including, where applicable, the requirements that (i) any reimbursement is for expenses incurred during Executive's lifetime (or during a shorter period of time specified in this Agreement), (ii) the amount of expenses eligible for reimbursement during a calendar year may not affect the expenses eligible for reimbursement in any other calendar year, (iii) the reimbursement of an eligible expense will be made on or before the last day of the calendar year following the year in which the expense is incurred and (iv) the right to reimbursement is not subject to set off or liquidation or exchange for any other benefit.

(vi) Notwithstanding anything herein to the contrary, the Company shall have no liability to Executive or to any other person if the payments and benefits provided hereunder that are intended to be exempt from or compliant with Section 409A are not so exempt or compliant.

(e) Modified Section 280G Cutback.

(i) Notwithstanding any other provision of this Agreement, except as set forth in Section 4(e)(ii), in the event that the Company undergoes a "Change in Ownership or Control" (as defined below), the Company shall not be obligated to provide to Executive a portion of any "Contingent Compensation Payments" (as defined below) that Executive would otherwise be entitled to receive to the extent necessary to eliminate any "excess parachute payments" (as defined in Section 280G(b)(1) of the Code) for Executive. For purposes of this Section 4(e), the Contingent Compensation Payments so eliminated shall be referred to as the "Eliminated Payments" and the aggregate amount (determined in accordance with Treasury Regulation Section 1.280G-1, Q/A-30 or any successor provision) of the Contingent Compensation Payments so eliminated shall be referred to as the "Eliminated Amount."

(ii) Notwithstanding the provisions of Section 4(e)(i), no such reduction in Contingent Compensation Payments shall be made if (1) the Eliminated Amount (computed without regard to this sentence) exceeds (2) 100% of the aggregate present value (determined in accordance with Treasury Regulation Section 1.280G-1, Q/A-31 and Q/A-32 or any successor provisions) of the amount of any additional taxes that would be incurred by Executive if the Eliminated Payments (determined without regard to this sentence) were paid to him (including federal and state income taxes on the Eliminated Payments, the excise tax imposed by Section 4999 of the Code payable with respect to all of the Contingent Compensation Payments in excess of Executive's "base amount" (as defined in Section 280G(b)(3) of the Code), and any withholding taxes). The override of such reduction in Contingent Compensation Payments pursuant to this Section 4(e)(ii) shall be referred to as a "Section 4(e)(ii) Override." For purpose of this paragraph, if any federal or state income taxes would be attributable to the receipt of any

Eliminated Payment, the amount of such taxes shall be computed by multiplying the amount of the Eliminated Payment by the maximum combined federal and state income tax rate provided by law.

(iii) For purposes of this Section 4(e) the following terms shall have the following respective meanings:

(1) "Change in Ownership or Control" shall mean a change in the ownership or effective control of the Company or in the ownership of a substantial portion of the assets of the Company determined in accordance with Section 280G(b)(2) of the Code.

(2) "Contingent Compensation Payment" shall mean any payment (or benefit) in the nature of compensation that is made or made available (under this Agreement or otherwise) to a "disqualified individual" (as defined in Section 280G(c) of the Code) and that is contingent (within the meaning of Section 280G(b)(2)(A)(i) of the Code) on a Change in Ownership or Control of the Company.

(iv) Any payments or other benefits otherwise due to Executive following a Change in Ownership or Control that could reasonably be characterized (as determined by the Company) as Contingent Compensation Payments (the "Potential Payments") shall not be made until the dates provided for in this Section 4(e)(iv). Within 30 days after each date on which Executive first becomes entitled to receive (whether or not then due) a Contingent Compensation Payment relating to such Change in Ownership or Control, the Company shall determine and notify Executive (with reasonable detail regarding the basis for its determinations) (1) which Potential Payments constitute Contingent Compensation Payments, (2) the Eliminated Amount and (3) whether the Section 4(e)(ii) Override is applicable. Within 30 days after delivery of such notice to Executive, Executive shall deliver a response to the Company (the "Executive Response") stating either (A) that he agrees with the Company's determination pursuant to the preceding sentence or (B) that he disagrees with such determination, in which case he shall set forth (x) which Potential Payments should be characterized as Contingent Compensation Payments, (y) the Eliminated Amount, and (z) whether the Section 4(e)(ii) Override is applicable. In the event that Executive fails to deliver an Executive Response on or before the required date, the Company's initial determination shall be final. If Executive states in the Executive Response that he agrees with the Company's determination, the Company shall make the Potential Payments to Executive within three business days following delivery to the Company of the Executive Response (except for any Potential Payments which are not due to be made until after such date, which Potential Payments shall be made on the date on which they are due). If Executive states in the Executive Response that he disagrees with the Company's determination, then, for a period of 60 days following delivery of the Executive Response, Executive and the Company shall use good faith efforts to resolve such dispute. If such dispute is not resolved within such 60-day period, such dispute shall be settled exclusively by arbitration in the greater Boston, Massachusetts area, in accordance with the rules of the American Arbitration Association then in effect. Judgment may be entered on the arbitrator's award in any court having jurisdiction. The Company shall, within three business days following delivery to the Company of the Executive Response, make to

Executive those Potential Payments as to which there is no dispute between the Company and Executive regarding whether they should be made (except for any such Potential Payments which are not due to be made until after such date, which Potential Payments shall be made on the date on which they are due). The balance of the Potential Payments shall be made within three business days following the resolution of such dispute.

(v) The Contingent Compensation Payments to be treated as Eliminated Payments shall be determined by the Company by determining the "Contingent Compensation Payment Ratio" (as defined below) for each Contingent Compensation Payment and then reducing the Contingent Compensation Payments in order beginning with the Contingent Compensation Payment with the highest Contingent Compensation Payment Ratio. For Contingent Compensation Payments with the same Contingent Compensation Payment Ratio, such Contingent Compensation Payment shall be reduced based on the time of payment of such Contingent Compensation Payments with amounts having later payment dates being reduced first. For Contingent Compensation Payments with the same Contingent Compensation Payment Ratio and the same time of payment, such Contingent Compensation Payments shall be reduced on a pro rata basis (but not below zero) prior to reducing Contingent Compensation Payments with a lower Contingent Compensation Payment Ratio. The term "Contingent Compensation Payment Ratio" shall mean a fraction the numerator of which is the value of the applicable Contingent Compensation Payment that must be taken into account by Executive for purposes of Section 4999(a) of the Code, and the denominator of which is the actual amount to be received by Executive in respect of the applicable Contingent Compensation Payment. For example, in the case of an equity grant that is treated as contingent on the Change in Ownership or Control because the time at which the payment is made or the payment vests is accelerated, the denominator shall be determined by reference to the fair market value of the equity at the acceleration date, and not in accordance with the methodology for determining the value of accelerated payments set forth in Treasury Regulation Section 1.280G-1Q/A-24(b) or (c)).

(vi) The provisions of this Section 4(e) are intended to apply to any and all payments or benefits available to Executive under this Agreement or any other agreement or plan of the Company under which Executive receives Contingent Compensation Payments.

5. Employee Covenants.

(a) Confidential Information. Executive recognizes and acknowledges the competitive and proprietary aspects of the business of the Company, and that as a result of Executive's employment, Executive recognizes and acknowledges that he has had and will continue to have access to, and has been and will continue to be involved in the development of, Confidential Information (as defined below) of the Company. As used herein, "Confidential Information" shall mean and include trade secrets, knowledge and other confidential information of the Company, which Executive has acquired, no matter from whom or on what matter such knowledge or information may have been acquired, heretofore or hereafter, concerning the content and details of the business of the Company, and which is not known to the general public, including but not limited to: confidential and proprietary information supplied to Executive with the legend "Confidential and Proprietary," or equivalent, the Company's marketing and customer support strategies, suppliers and customers, marketing and selling,

business plans, licenses, the Company's financial information, including sales, costs, profits, prices, pricing methods, budgets and unpublished financial statements, the Company's internal organization, employee information obtained pursuant to Executive's duties and responsibilities, information regarding the skills and compensation of other employees of the Company obtained pursuant to Executive's duties and responsibilities and customer lists, the Company's technology, including products, discoveries, inventions, research, experimental and development efforts, clinical studies, processes, hardware/software design and maintenance tools, samples, media and/or molecular structures (and procedures and formulations for producing any such samples, media and/or molecular structures), formulas, methods, know-how and show-how, designs, prototypes, plans for research and new products, and all derivatives, improvements and enhancements of any of the above and information of third parties as to which the Company has an obligation of confidentiality.

(i) For as long as Executive is employed and at all times thereafter, Executive shall not, directly or indirectly, communicate, disclose or divulge to any person or entity, or use for Executive's own benefit or the benefit of any person (other than the Company), any Confidential Information, except as permitted in subparagraph (iii) below. Upon termination of Executive's employment, or at any other time at the request of the Company, Executive agrees to deliver promptly to the Company all Confidential Information, including, but not limited to, customer and supplier lists, files and records, in Executive's possession or under Executive's control. Executive further agrees that he will not make or retain any copies of any of the foregoing and will so represent to the Company upon termination of Executive's employment.

(ii) Executive shall disclose immediately to the Company any Confidential Information conceived or developed by Executive at any time during Executive's employment. Executive hereby assigns and agrees to assign to the Company Executive's entire right, title and interest in and to all Confidential Information. Such assignment shall include, without limitation, the rights to obtain patent or copyright protection thereon in the United States and foreign countries. Executive agrees to provide all reasonable assistance to enable the Company to prepare and prosecute any application before any governmental agency for patent or copyright protection or any similar application with respect to any Confidential Information. Executive further agrees to execute all documents and assignments and to make all oaths necessary to vest ownership of such intellectual property rights in the Company, as the Company may request. These obligations shall apply whether or not the subject thereof was conceived or developed at the suggestion of the Company, and whether or not developed during regular hours of work or while on the premises of the Company.

(iii) Except as set forth below, Executive shall at all times, both during and after termination of this Agreement by either Executive or the Company, maintain in confidence and shall not, without prior written consent of the Company, use, except in the course of performance of Executive's duties for the Company or as required by legal process (provided that Executive will promptly notify the Company of such legal process except with respect to any confidential government investigation), disclose or give to others any Confidential Information. In the event Executive is questioned by anyone not employed by the Company or by an employee of or a consultant to the Company not authorized to receive Confidential Information, in regard to any such Confidential Information, or concerning any fact or circumstance relating thereto, Executive will

promptly notify the Company. Notwithstanding the foregoing, however, nothing in this Agreement or elsewhere prohibits Executive from communicating with government agencies about possible violations of federal, state, or local laws or otherwise providing information to government agencies, filing a complaint with government agencies, or participating in government agency investigations or proceedings. Executive is not required to notify the Company of any such communications; provided, however, that nothing herein authorizes the disclosure of information the Employee obtained through a communication that was subject to the attorney-client privilege. Further, notwithstanding Executive's confidentiality and nondisclosure obligations, Executive is hereby advised as follows pursuant to the Defend Trade Secrets Act: "An individual shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of a trade secret that (A) is made (i) in confidence to a Federal, State, or local government official, either directly or indirectly, or to an attorney; and (ii) solely for the purpose of reporting or investigating a suspected violation of law; or (B) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal. An individual who files a lawsuit for retaliation by an employer for reporting a suspected violation of law may disclose the trade secret to the attorney of the individual and use the trade secret information in the court proceeding, if the individual (A) files any document containing the trade secret under seal; and (B) does not disclose the trade secret, except pursuant to court order."

(b) Non-Competition and Non-Solicitation. Executive recognizes that the Company is engaged in a competitive business and that the Company has a legitimate interest in protecting its trade secrets, confidential business information, and customer, business development partner, licensee, supplier, and credit and/or financial relationships. Accordingly, in exchange for valuable consideration, including without limitation Executive's access to confidential business information and continued at-will employment, Executive agrees that, during the Term hereof and for a period of twelve (12) months thereafter, Executive shall not:

(i) directly or indirectly, whether for himself or for any other person or entity, and whether as a proprietor, principal, shareholder, partner, agent, employee, consultant, independent contractor, or in any other capacity whatsoever, undertake or have any interest in (other than the passive ownership of publicly registered securities representing an ownership interest of less than 1%), engage in or assume any role involving directly or indirectly any business activity which is directly or indirectly in competition with the products or services being developed, marketed, sold or otherwise provided by the Company or any other business in which the Company is engaged and for which Executive has rendered services while employed by the Company, or enter into any agreement to do any of the foregoing; or

(ii) initiate contact with (including without limitation phone calls, press releases and the sending or delivering of announcements), or in any manner solicit, directly or indirectly, any customers, business development partners, licensors, licensees, or creditors (including institutional lenders, bonding companies and trade creditors) of the Company in an attempt to induce or motivate them either to discontinue or modify their then prevailing or future relationship with the Company or to transfer any of their business with the Company to any person or entity other than the Company; or

(iii) initiate contact with, or in any manner solicit, directly or indirectly, any supplier of goods, services or materials to the Company in an attempt to induce or motivate them either to discontinue or modify their then prevailing or future relationship with the Company or to supply the same or similar inventory, goods, services or materials (except generally available inventory, goods, services or materials) to any person or entity other than the Company; or

(iv) directly or indirectly recruit, solicit or otherwise induce or influence any employee or independent contractor of the Company to discontinue or modify his or her employment or engagement with the Company, or employ or contract with any such employee or contractor for the provision of services.

(c) Definition of "Customer". The term "customer" or "customers" shall include any person or entity (a) that is a current customer of the Company, (b) that was a customer of the Company at any time during the preceding twenty-four (24) months or (c) to which the Company made a written presentation for the solicitation of business at any time during the preceding twenty-four (24) months.

(d) Reasonableness of Restrictions. Executive further recognizes and acknowledges that (i) the types of employment which are prohibited by this Section 5 are narrow and reasonable in relation to the skills which represent Executive's principal salable asset both to the Company and to Executive's other prospective employers, and (ii) the broad geographical scope of the provisions of this Section 5 is reasonable, legitimate and fair to Executive in light of the global nature of the Company's business, and in light of the limited restrictions on the type of employment prohibited herein compared to the types of employment for which Executive is qualified to earn Executive's livelihood.

(e) Remedies. Executive acknowledges that a breach of this Section 5 is likely to cause great and irreparable injury and damage, which cannot be reasonably or adequately compensated by money damages. Accordingly, Executive acknowledges that the remedies of injunction and specific performance shall be available in the event of such a breach, in addition to money damages, costs and attorneys' fees, and other legal or equitable remedies, and that the Company shall be entitled as a matter of course to an injunction pending trial, without the posting of bond or other security. Any period of restriction set forth in this Section 5 shall be extended for a period of time equal to the duration of any breach or violation hereof.

(f) Notification. Any person employing Executive or evidencing any intention to employ Executive may be notified as to the existence and provisions of this Agreement.

(g) Modification of Covenants; Enforceability. In the event that any provision of this Section 5 is held to be in any respect an unreasonable restriction, then the court so holding may modify the terms thereof, including the period of time during which it operates or the geographic area to which it applies, or effect any other change to the extent necessary to render this section enforceable, it being acknowledged by the parties that the representations and covenants set forth herein are of the essence of this Agreement.

(h) Subsidiaries. For purposes of Sections 5 and 6 of this Agreement, "Company" shall include all subsidiaries of the Company. An entity shall be deemed to be a subsidiary of the Company if the Company directly or indirectly owns or controls 50% or more of the equity interest in such entity.

6. Ownership of Ideas, Copyrights and Patents.

(a) Property of the Company. Executive agrees that all ideas, inventions, original works of authorship, developments, concepts, know-how, improvements or trade secrets, whether patentable, copyrightable or not, which Executive may conceive, reduce to practice or develop, alone or in conjunction with another, or others, whether during or out of regular business hours, and whether at the request or upon the suggestion of the Company, or otherwise, in the course of performing services for the Company in any capacity, whether heretofore or hereafter, (collectively, "the Inventions") are and shall be the sole and exclusive property of the Company, and that Executive shall not publish any of the Inventions without the prior written consent of the Company. Executive hereby assigns to the Company all of Executive's right, title and interest in and to all of the foregoing. Executive further represents and agrees that to the best of Executive's knowledge and belief none of the Inventions will violate or infringe upon any right, patent, copyright, trademark or right of privacy, or constitute libel or slander against or violate any other rights of any person, firm or corporation and that Executive will use his best efforts to prevent any such violation.

(b) Cooperation. At any time during or after the Term, Executive agrees that he will fully cooperate with the Company, its attorneys and agents in the preparation and filing of all papers and other documents as may be required to perfect the Company's rights in and to any of such Inventions, including, but not limited to, executing any lawful document (including, but not limited to, applications, assignments, oaths, declarations and affidavits) and joining in any proceeding to obtain letters patent, copyrights, trademarks or other legal rights of the United States and of any and all other countries on such Inventions, provided that any patent or other legal right so issued to Executive, personally, shall be assigned by Executive to the Company without charge by Executive. Executive further designates the Company as his agent for, and grants to the Company a power of attorney with full power of substitution, which power of attorney shall be deemed coupled with an interest, for the purpose of effecting the foregoing assignments from Executive to the Company. Company will bear the reasonable expenses which it causes to be incurred in Executive's assisting and cooperating hereunder. Executive waives all claims to moral rights in any Inventions.

7. Disclosure to Future Employers. The Company may provide in its discretion, a copy of the covenants contained in Sections 5 and 6 of this Agreement to any business or enterprise which Executive may directly, or indirectly, own, manage, operate, finance, join, control or in which Executive participates in the ownership, management, operation, financing, or control, or with which Executive may be connected as an officer, director, employee, partner, principal, agent, representative, consultant or otherwise.

8. Records. Upon termination of Executive's employment with the Company, Executive shall deliver to the Company any property of the Company which may be in Executive's possession including products, materials, memoranda, notes, records, reports, or other documents or photocopies of the same.

9. Insurance. The Company, in its sole discretion, may apply for and procure in its own name (whether or not for its own benefit) policies of insurance insuring Executive's life. Executive agrees to submit to reasonable medical or other examinations and to execute and deliver any applications or other instruments in writing that are reasonably necessary to effectuate such insurance. No adverse employment actions may be based upon the results of any such exam or the failure by the Company to obtain such insurance.

10. No Conflicting Agreements. Executive hereby represents and certifies that Executive has no commitments or obligations inconsistent with this Agreement.

11. Conditions to Employment. Notwithstanding anything to the contrary contained herein, this Agreement and Executive's employment hereunder is subject to and conditioned on reference checks, and Executive's provision of proof of his right to work in the United States.

12. General.

(a) Notices. All notices, requests, consents and other communications hereunder shall be in writing, shall be addressed to the receiving party's address as follows:

If to the Company: Ocular Therapeutix, Inc.
36 Crosby Drive, Suite 101
Bedford, MA 01730
USA
Attention: Chief Executive Officer
Telephone: (781) 357-4000

With an email copy to: ASawhney@ocutx.com

If to Executive: Daniel Bollag
7 Apollo Circle, Lexington, MA 02421

or to such other address as a party may designate by notice hereunder, and shall be either (i) delivered by hand, (ii) sent by overnight courier, or (iii) sent by registered or certified mail, return receipt requested, postage prepaid. All notices, requests, consents and other communications hereunder shall be deemed to have been given either (i) if by hand, at the time of the delivery thereof to the receiving party at the address of such party set forth above, (ii) if sent by overnight courier, on the next business day following the day such notice is delivered to the courier service, or (iii) if sent by registered or certified mail, on the fifth (5th) business day following the day such mailing is made.

(b) Entire Agreement. This Agreement embodies the entire agreement and understanding between the parties hereto with respect to the subject matter hereof and supersedes all prior oral or written agreements and understandings relating to the subject matter hereof. No statement, representation, warranty, covenant or agreement of any kind not expressly set forth in this Agreement shall affect, or be used to interpret, change or restrict, the express terms and provisions of this Agreement.

(c) Modifications and Amendments. The terms and provisions of this Agreement may be modified or amended only by written agreement executed by the parties hereto.

(d) Waivers and Consents. The terms and provisions of this Agreement may be waived, or consent for the departure therefrom granted, only by written document executed by the party entitled to the benefits of such terms or provisions. No such waiver or consent shall be deemed to be or shall constitute a waiver or consent with respect to any other terms or provisions of this Agreement, whether or not similar. Each such waiver or consent shall be effective only in the specific instance and for the purpose for which it was given, and shall not constitute a continuing waiver or consent.

(e) Assignment. The Company shall assign its rights and obligations hereunder to any person or entity that succeeds to all or substantially all of the Company's business or that aspect of the Company's business in which Executive is principally involved. Executive may not assign Executive's rights and obligations under this Agreement without the prior written consent of the Company.

(f) Benefit. All statements, representations, warranties, covenants and agreements in this Agreement shall be binding on the parties hereto and shall inure to the benefit of the respective successors and permitted assigns of each party hereto. Nothing in this Agreement shall be construed to create any rights or obligations except among the parties hereto, and no person or entity shall be regarded as a third-party beneficiary of this Agreement.

(g) Governing Law. This Agreement and the rights and obligations of the parties hereunder shall be construed in accordance with and governed by the law of the Commonwealth of Massachusetts, without giving effect to the conflict of law principles thereof.

(h) Jurisdiction and Service of Process. Any legal action or proceeding with respect to this Agreement shall be brought in the courts of The Commonwealth of Massachusetts or of the United States of America for the District of Massachusetts. By execution and delivery of this Agreement, each of the parties hereto accepts for itself and in respect of its property, generally and unconditionally, the jurisdiction of the aforesaid courts. Each of the parties hereto irrevocably consents to the service of process of any of the aforementioned courts in any such action or proceeding by the mailing of copies thereof by certified mail, postage prepaid, to the party at its address set forth in Section 12(a) hereof. THE PARTIES IRREVOCABLY WAIVE ANY RIGHT TO TRIAL BY JURY AS TO ALL CLAIMS HEREUNDER.

(i) Severability. The parties intend this Agreement to be enforced as written. However, (i) if any portion or provision of this Agreement shall to any extent be declared illegal or unenforceable by a duly authorized court having jurisdiction, then the remainder of this Agreement, or the application of such portion or provision in circumstances other than those as to which it is so declared illegal or unenforceable, shall not be affected thereby, and each portion and provision of this Agreement shall be valid and enforceable to the fullest extent permitted by law; and (ii) if any provision, or part thereof, is held to be unenforceable because of the duration of such provision or the geographic area covered thereby, the Company and Executive agrees that the court making such determination shall have the power to reduce the duration and/or geographic area of such provision, and/or to delete specific words and phrases ("blue-

penciling"), and in its reduced or blue-penciled form such provision shall then be enforceable and shall be enforced.

(j) Headings and Captions; Interpretation. The headings and captions of the various subdivisions of this Agreement are for convenience of reference only and shall in no way modify, or affect the meaning or construction of any of the terms or provisions hereof. The provisions of the following Sections of this Agreement are in addition to, and do not limit, each other: Sections 6 and 5(a); Sections 7 and 5(g); Sections 12(k) and 5(f); and Sections 12(l) and 12(d).

(k) Injunctive Relief. Executive hereby expressly acknowledges that any breach or threatened breach of any of the terms and/or conditions set forth in Section 5 or 6 of this Agreement is likely to result in substantial, continuing and irreparable injury to the Company. Therefore, Executive hereby agrees that, in addition to any other remedy that may be available to the Company, the Company shall be entitled to injunctive or other equitable relief by a court of appropriate jurisdiction.

(l) No Waiver of Rights, Powers and Remedies. No failure or delay by a party hereto in exercising any right, power or remedy under this Agreement, and no course of dealing between the parties hereto, shall operate as a waiver of any such right, power or remedy of the party. No single or partial exercise of any right, power or remedy under this Agreement by a party hereto, nor any abandonment or discontinuance of steps to enforce any such right, power or remedy, shall preclude such party from any other or further exercise thereof or the exercise of any other right, power or remedy hereunder. The election of any remedy by a party hereto shall not constitute a waiver of the right of such party to pursue other available remedies. No notice to or demand on a party not expressly required under this Agreement shall entitle the party receiving such notice or demand to any other or further notice or demand in similar or other circumstances or constitute a waiver of the rights of the party giving such notice or demand to any other or further action in any circumstances without such notice or demand.

(m) Counterparts. This Agreement may be executed in one or more counterparts, and by different parties hereto on separate counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

(n) Survival. The provisions of Sections 4, 5, 6, 7, 8, and 12 shall survive the termination of this Agreement and Executive's employment hereunder in accordance with their terms.

IN WITNESS THEREOF, the parties hereto have executed this Agreement as of the day and year first above written.

Ocular Therapeutix, Inc.

/s/ Amar Sawhney
Name: Amar Sawhney
Title: President & Chief Executive Officer

Agreed and Accepted

/s/ Daniel Bollag
Daniel Bollag

Exhibit 10.30

EMPLOYMENT AGREEMENT

This EMPLOYMENT AGREEMENT (the "Agreement") is made as of September 5, 2017 (the "Effective Date"), by and between Ocular Therapeutix, Inc., a Delaware corporation (the "Company"), and Michael Goldstein ("Executive"). In consideration of the mutual covenants contained in this Agreement, the Company and Executive agree as follows:

1. Employment. The Company agrees to employ Executive and Executive agrees to be employed by the Company on the terms and conditions set forth in this Agreement.

(a) Capacity. Executive shall serve the Company as Chief Medical Officer, reporting to the Company's Chief Executive Officer (the "CEO"). During the Term (as defined below) of Executive's employment with the Company, Executive shall, subject to the direction of the CEO, have the responsibilities, duties and authority commensurate with the position of Chief Medical Officer and shall perform such other duties as may from time to time be assigned to him by the Company. The Company may change Executive's duties and work location as it deems necessary.

(b) Devotion of Duties; Representations. During the Term of Executive's employment with the Company, Executive shall devote his best efforts and at least 80% of his full business time and energies to the business and affairs of the Company, and shall endeavor to perform the duties and services contemplated hereunder to the reasonable satisfaction of the Company. During the Term of Executive's employment with the Company, Executive shall not, without the prior written approval of the Company (by action of the Company's Board of Directors (the "Board")), undertake any other employment from any person or entity or serve as a director of any other company; provided, however, that (i) the Company will entertain requests as to such other employment or directorships in good faith and (ii) Executive will be eligible to participate in any policy relating to outside activities that is applicable to the senior executives of the Company and approved by the Board after the date hereof, and provided further that in no event may any business activity be undertaken if it would (x) be in violation of any provision of this Agreement or other agreement between Executive and the Company, (y) interfere with the performance of Executive's duties for the Company, or (z) present a conflict of interest with the Company's business interests. For the avoidance of doubt, the Company acknowledges that Executive may continue to practice medicine on an average of one (1) day per week and may enter into business arrangements that allow him to do so, provided that such arrangements do not interfere with the performance of Executive's duties for the Company or present a conflict of interest with the Company's business interests.

2. Term of Employment.

(a) Executive's employment hereunder shall begin on the Effective Date. Executive's employment hereunder shall be terminated upon the first to occur of the following:

(i) Immediately upon Executive's death;

(ii) By the Company, by written notice to Executive effective as of the date of such notice (or on such other date as specified in such notice):

(A) Following the Disability of Executive. "Disability" means that Executive is unable to perform his duties hereunder by reason of any mental, physical or other disability for a period of at least three (3) months, as determined by a qualified physician. Notwithstanding the foregoing, for any payments or benefits hereunder or pursuant to any other agreement between the Company and Executive, in either case that are subject to Section 409A of the Internal Revenue Code of 1986, as amended (the "Code") and the guidance issued thereunder, such Disability must result in Executive becoming "Disabled" within the meaning of Section 409A(a)(2)(C) of the Code. (In this Agreement we refer to Section 409A of the Code and any guidance issued thereunder as "Section 409A.")

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

(C) Subject to Section 4 hereof, without Cause;

(iii) By Executive:

(A) At any time by written notice to the Company, effective thirty (30) days after the date of such notice; or

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

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

(b) Definition of "Cause". For purposes of this Agreement, "Cause" shall, pursuant to the reasonable good faith determination by the Company as documented in writing, mean: (i) the willful and continued failure by Executive to substantially perform Executive's material duties or responsibilities under this Agreement (other than such a failure as a result of Disability); (ii) any action or omission by Executive involving willful misconduct or gross negligence with regard to the Company, which has a detrimental effect on the Company; (iii) Executive's conviction of a felony, either in connection with the performance of Executive's obligations to the Company or which otherwise shall adversely affect Executive's ability to perform such obligations or shall materially adversely affect the business activities, reputation, goodwill or image of the Company; (iv) the material breach of a fiduciary duty to the Company; or (v) the material breach by Executive of any of the provisions of this Agreement, provided that any breach of Executive's obligations with respect to Sections 5 or 6 of this Agreement, subject to the cure provision in the next sentence, shall be deemed "material." In respect of the events described in clauses (i) and (v) above, the Company shall give Executive notice of the failure of performance or breach, reasonable as to time, place and manner in the circumstances, and a 30-day opportunity to cure, provided that such failure of performance or breach is reasonably amenable to cure as determined by the Company in its sole discretion.

(c) Definition of "Good Reason". For purposes of this Agreement, a "Good Reason" shall mean any of the following, unless (i) the basis for such Good Reason is cured within a reasonable period of time (determined in the light of the cure appropriate to the basis of such Good Reason, but in no event less than thirty (30) nor more than ninety (90) days) after the Company receives written notice (which must be received from Executive within ninety (90) days of the initial

existence of the condition giving rise to such Good Reason) specifying the basis for such Good Reason or (ii) Executive has consented to the condition that would otherwise be a basis for Good Reason:

(i) A change in the principal location at which Executive provides services to the Company to a location more than fifty (50) miles from such principal location (which change, the Company has reasonably determined as of the date hereof, would constitute a material change in the geographic location at which Executive provides services to the Company), provided that such a relocation shall not be deemed to occur under circumstances where Executive's responsibilities require him to work at a location other than the corporate headquarters for a reasonable period of time;

(ii) A material adverse change by the Company in Executive's duties, authority or responsibilities which causes Executive's position with the Company to become of materially less responsibility or authority than Executive's position immediately following the Effective Date where such change is not remedied within ten (10) business days after written notice thereof by Executive;

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

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

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

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

entitled to vote generally in the election of directors, respectively, of the resulting or acquiring corporation in substantially the same proportions as their ownership of the Company's outstanding shares immediately prior to the merger, consolidation, reorganization or restructuring. Notwithstanding the foregoing, for any payments or benefits hereunder (including pursuant to Section 4(b)(iii) hereof) or pursuant to any other agreement between the Company and Executive, in either case that are subject to Section 409A, the Corporate Change must constitute a "change in control event" within the meaning of Treasury Regulation Section 1.409A-3(i)(5)(i).

3. Compensation.

(a) Base Salary. Executive's minimum base salary during the Term shall be at the rate of $400,000 per year. Executive's base salary shall be payable in substantially equal installments in accordance with the Company's payroll practices as in effect from time to time, less any amounts required to be withheld under applicable law. The base salary will be subject to adjustment from time to time in the sole discretion of the Company; provided that, the Company covenants that (A) during the first twelve (12) months of Executive's employment, it shall not reduce Executive's base salary and (B) following such twelve-month period, it shall not reduce the base salary below the base salary then in effect immediately prior to the reduction unless (i) Executive consents to such reduction, or (ii) the reduction is in connection with a general reduction of not more than 20% in compensation of senior executives of the Company generally that occurs prior to the effective date of any Corporate Change.

(b) Bonus. In addition to the base salary, the Company may pay Executive an annual bonus (the "Bonus") as determined by the Board, solely in its discretion (it being understood that Executive's target annual bonus shall be 35% of Executive's base salary in effect for such year, but may be higher or lower in any year in the Board's discretion). The Board's decision to issue a Bonus to Executive in any particular year shall have no effect on the absolute discretion of the Board to grant or not to grant a Bonus in subsequent years. Executive must be an active employee of the Company on December 31 of any calendar year in order to be eligible for and to earn any Bonus for that year. Any Bonus for a particular year shall be paid or provided to Executive in a lump sum no later than March 15th of the calendar year following the calendar year in which the Bonus was earned. For the avoidance of doubt, any Bonus for the 2017 calendar year would be prorated.

(c) Stock Option Grant. Subject to approval by the Board, the Company will grant to Executive an option to purchase 135,000 shares of the Company's common stock (the "Option"). The Option is subject to adjustment for stock splits, combinations or other recapitalizations. The exercise price per share of the Option shall be equal to the last reported sale price per share of the common stock on the NASDAQ stock exchange on the effective date of grant of the Option approved by the Board. The Option shall be issued pursuant to the Company's 2014 Equity Incentive Plan, as it may be amended from time to time, and will be subject to all of the terms and conditions set forth in such plan and the Stock Option Agreement covering the Option.

(d) Vacation. Executive shall be entitled to take sixteen (16) days of paid vacation during each year of the Term to be taken at such time or times as shall be mutually convenient and consistent with his duties and obligations to the Company. The number of vacation days for which Executive is eligible shall accrue at the rate of 1.5 days per month.

Vacation is at all times subject to the Company's Time-Off Policy, which the Company may change periodically in its sole discretion.

(e) Fringe Benefits. Executive shall be entitled to participate in any employee benefit plans that the Company makes available to its executives (including, without limitation, group life, disability, medical, dental and other insurance, retirement, pension, profit-sharing and similar plans) (collectively, the "Fringe Benefits"), provided that the Fringe Benefits shall not include any stock option or similar plans relating to the grant of equity securities of the Company. These benefits may be modified or changed from time to time at the sole discretion of the Company. Where a particular benefit is subject to a formal plan (for example, medical or life insurance), eligibility to participate in and receive any particular benefit is governed solely by the applicable plan document, and eligibility to participate in such plan(s) may be dependent upon, among other things, a physical examination.

(f) Reimbursement of Expenses. Executive shall be entitled to reimbursement for all ordinary and reasonable out-of-pocket business expenses that are reasonably incurred by him in furtherance of the Company's business in accordance with reasonable policies adopted from time to time by the Company for senior executives, subject to Section 4(d)(v).

4. Severance Compensation.

(a) In the event of any termination of Executive's employment for any reason, the Company shall pay Executive (or Executive's estate) such portions of Executive's base salary as have accrued prior to such termination and have not yet been paid, together with (i) amounts for accrued unused vacation days (as provided above), (ii) any amounts for expense reimbursement which have been properly incurred or the Company has become obligated to pay prior to termination and have not been paid as of the date of such termination and (iii) the amount of any Bonus previously granted to Executive by the Board but not yet paid, which amount shall not include any pro rata portion of any Bonus which would have been earned if such termination had not occurred (the "Accrued Obligations"). Such Accrued Obligations shall be paid as soon as possible after termination, and in any event in accordance with applicable law.

(b) In the event that Executive's employment hereunder is terminated (i) by Executive for a Good Reason or (ii) by the Company without Cause, the Company shall pay to Executive the Accrued Obligations. In addition, the Company shall pay to Executive the severance benefits set forth below for twelve (12) months, or for eighteen (18) months if such termination occurs during the twelve (12) month period following a Corporate Change (the "Protected Period"), following Executive's termination of employment (as applicable, the "Severance Period"). The receipt of any severance benefits provided in this Section shall be dependent upon Executive's execution and, to the extent applicable, nonrevocation of the Company's standard separation and general release of claims agreement, the substantive provisions of which will be: Executive's non-disparagement, confidentiality, and cooperation obligations; Executive's release of all releasable claims arising out of or relating to his employment with the Company, his separation of employment from the Company, any officer or director position(s) he may hold or have held with the Company, any and all compensation and benefits he received from the Company, and any and all agreements he entered into with the Company (provided, however, that the release shall not affect any rights Executive may have for indemnification); reaffirmation of Executive's existing restrictive covenant obligations; Executive's

acknowledgement of receipt of all business expense reimbursements and final compensation; and Executive's acknowledgement that he has returned to the Company all Company property and confidential information (the "Release"), which Release must be signed and any applicable revocation period with respect thereto must have expired by the sixtieth (60th) day following Executive's termination of employment. The severance benefits shall be paid or commence, as applicable, on the first payroll period following the date the Release becomes effective (the "Payment Date"). Notwithstanding the foregoing, if the 60th day following Executive's termination occurs in the calendar year following the date on which Executive's employment terminates, then the Payment Date shall be no earlier than January 1 of such subsequent calendar year.

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

(ii) Only if Executive's employment is terminated (A) by Executive for a Good Reason or (B) by the Company without Cause, in each case during the Protected Period, the Company shall pay Executive an amount equal to one and one-half times his target annual bonus, described in Section 3(b) hereof, for the year in which the termination of employment occurs, which total amount shall be payable in a lump sum on the Payment Date.

(iii) Only if Executive's employment is terminated (A) by Executive for a Good Reason or (B) by the Company without Cause, in each case during the Protected Period, one hundred percent (100%) of Executive's outstanding unvested equity awards granted under the Company's equity and long-term incentive plan(s) prior to his termination shall vest immediately.

(iv) The Company shall continue to provide Executive and his then-enrolled eligible spouse and dependents with group health insurance and shall continue to pay the amount of the premium as in effect on the date of such termination for the Severance Period commencing on the effective date of such termination, subject to applicable law and the terms of the respective policies; provided that the Company's obligation to provide the benefits contemplated herein shall terminate upon Executive's becoming eligible for coverage under the medical benefits program of a subsequent employer. The foregoing shall not be construed to extend any period of continuation coverage (e.g., COBRA) required by Federal law.

(c) In the event that Executive's employment hereunder is terminated (i) by Executive for other than a Good Reason, or (ii) by the Company for Cause, or (iii) as a result of Executive's death or Disability, then the Company will pay to Executive the Accrued Obligations. The Company shall have no obligation to pay Executive (or Executive's estate) any other compensation following such termination except as provided in Section 4(a).

(d) Compliance with Section 409A. Subject to the provisions in this Section 4(d), any severance payments or benefits under this Agreement shall begin only upon the date of Executive's "separation from service" (determined as set forth below) which occurs on or after

the date of termination of Executive's employment. The following rules shall apply with respect to the distribution of the severance payments and benefits, if any, to be provided to Executive under this Agreement:

(i) It is intended that each installment of the severance payments and benefits provided under this Agreement shall be treated as a separate "payment" for purposes of Section 409A. Neither the Company nor Executive shall have the right to accelerate or defer the delivery of any such payments or benefits except to the extent specifically permitted or required by Section 409A.

(ii) If, as of the date of Executive's "separation from service" from the Company, Executive is not a "specified employee" (within the meaning of Section 409A), then each installment of the severance payments and benefits shall be made on the dates and terms set forth in this Agreement.

(iii) If, as of the date of Executive's "separation from service" from the Company, Executive is a "specified employee" (within the meaning of Section 409A), then:

(A) Each installment of the severance payments and benefits due under this Agreement that, in accordance with the dates and terms set forth herein, will in all circumstances, regardless of when the separation from service occurs, be paid within the short-term deferral period (as defined under Section 409A) shall be treated as a short-term deferral within the meaning of Treasury Regulation Section 1.409A-1(b)(4) to the maximum extent permissible under Section 409A and such payments and benefits shall be paid or provided on the dates and terms set forth in this Agreement; and

(B) Each installment of the severance payments and benefits due this Agreement that is not described in Section 4(d)(iii)(A) above and that would, absent this subsection (B), be paid within the six-month period following Executive's "separation from service" from the Company shall not be paid until the date that is six months and one day after such separation from service (or, if earlier, Executive's death), with any such installments that are required to be delayed being accumulated during the six-month period and paid in a lump sum on the date that is six months and one day following Executive's separation from service and any subsequent installments, if any, being paid in accordance with the dates and terms set forth herein; provided, however, that the preceding provisions of this sentence shall not apply to any installment of severance payments and benefits if and to the maximum extent that such installment is deemed to be paid under a separation pay plan that does not provide for a deferral of compensation by reason of the application of Treasury Regulation 1.409A-1(b)(9)(iii) (relating to separation pay upon an involuntary separation from service). Any installments that qualify for the exception under Treasury Regulation Section 1.409A-1(b)(9)(iii) must be paid no later than the last day of Executive's second taxable year following the taxable year in which the separation from service occurs.

(iv) The determination of whether and when Executive's separation from service from the Company has occurred shall be made in a manner consistent with, and based on the presumptions set forth in, Treasury Regulation Section 1.409A-1(h). Solely for purposes of this Section 4(d)(iv), "Company" shall include all persons with whom the Company would be considered a single employer under Section 414(b) and 414(c) of the Code.

(v) All reimbursements and in-kind benefits provided under this Agreement shall be made or provided in accordance with the requirements of Sections 409A to the extent that such reimbursements or in-kind benefits are subject to Section 409A, including, where applicable, the requirements that (i) any reimbursement is for expenses incurred during Executive's lifetime (or during a shorter period of time specified in this Agreement), (ii) the amount of expenses eligible for reimbursement during a calendar year may not affect the expenses eligible for reimbursement in any other calendar year, (iii) the reimbursement of an eligible expense will be made on or before the last day of the calendar year following the year in which the expense is incurred and (iv) the right to reimbursement is not subject to set off or liquidation or exchange for any other benefit.

(vi) Notwithstanding anything herein to the contrary, the Company shall have no liability to Executive or to any other person if the payments and benefits provided hereunder that are intended to be exempt from or compliant with Section 409A are not so exempt or compliant.

(e) Modified Section 280G Cutback.

(i) Notwithstanding any other provision of this Agreement, except as set forth in Section 4(e)(ii), in the event that the Company undergoes a "Change in Ownership or Control" (as defined below), the Company shall not be obligated to provide to Executive a portion of any "Contingent Compensation Payments" (as defined below) that Executive would otherwise be entitled to receive to the extent necessary to eliminate any "excess parachute payments" (as defined in Section 280G(b)(1) of the Code) for Executive. For purposes of this Section 4(e), the Contingent Compensation Payments so eliminated shall be referred to as the "Eliminated Payments" and the aggregate amount (determined in accordance with Treasury Regulation Section 1.280G-1, Q/A-30 or any successor provision) of the Contingent Compensation Payments so eliminated shall be referred to as the "Eliminated Amount."

(ii) Notwithstanding the provisions of Section 4(e)(i), no such reduction in Contingent Compensation Payments shall be made if (1) the Eliminated Amount (computed without regard to this sentence) exceeds (2) 100% of the aggregate present value (determined in accordance with Treasury Regulation Section 1.280G-1, Q/A-31 and Q/A-32 or any successor provisions) of the amount of any additional taxes that would be incurred by Executive if the Eliminated Payments (determined without regard to this sentence) were paid to him (including federal and state income taxes on the Eliminated Payments, the excise tax imposed by Section 4999 of the Code payable with respect to all of the Contingent Compensation Payments in excess of Executive's "base amount" (as defined in Section 280G(b)(3) of the Code), and any withholding taxes). The override of such reduction in Contingent Compensation Payments pursuant to this

Section 4(e)(ii) shall be referred to as a "Section 4(e)(ii) Override." For purpose of this paragraph, if any federal or state income taxes would be attributable to the receipt of any Eliminated Payment, the amount of such taxes shall be computed by multiplying the amount of the Eliminated Payment by the maximum combined federal and state income tax rate provided by law.

(iii) For purposes of this Section 4(e) the following terms shall have the following respective meanings:

(1) "Change in Ownership or Control" shall mean a change in the ownership or effective control of the Company or in the ownership of a substantial portion of the assets of the Company determined in accordance with Section 280G(b)(2) of the Code.

(2) "Contingent Compensation Payment" shall mean any payment (or benefit) in the nature of compensation that is made or made available (under this Agreement or otherwise) to a "disqualified individual" (as defined in Section 280G(c) of the Code) and that is contingent (within the meaning of Section 280G(b)(2)(A)(i) of the Code) on a Change in Ownership or Control of the Company.

(iv) Any payments or other benefits otherwise due to Executive following a Change in Ownership or Control that could reasonably be characterized (as determined by the Company) as Contingent Compensation Payments (the "Potential Payments") shall not be made until the dates provided for in this Section 4(e)(iv). Within 30 days after each date on which Executive first becomes entitled to receive (whether or not then due) a Contingent Compensation Payment relating to such Change in Ownership or Control, the Company shall determine and notify Executive (with reasonable detail regarding the basis for its determinations) (1) which Potential Payments constitute Contingent Compensation Payments, (2) the Eliminated Amount and (3) whether the Section 4(e)(ii) Override is applicable. Within 30 days after delivery of such notice to Executive, Executive shall deliver a response to the Company (the "Executive Response") stating either (A) that he agrees with the Company's determination pursuant to the preceding sentence or (B) that he disagrees with such determination, in which case he shall set forth (x) which Potential Payments should be characterized as Contingent Compensation Payments, (y) the Eliminated Amount, and (z) whether the Section 4(e)(ii) Override is applicable. In the event that Executive fails to deliver an Executive Response on or before the required date, the Company's initial determination shall be final. If Executive states in the Executive Response that he agrees with the Company's determination, the Company shall make the Potential Payments to Executive within three business days following delivery to the Company of the Executive Response (except for any Potential Payments which are not due to be made until after such date, which Potential Payments shall be made on the date on which they are due). If Executive states in the Executive Response that he disagrees with the Company's determination, then, for a period of 60 days following delivery of the Executive Response, Executive and the Company shall use good faith efforts to resolve such dispute. If such dispute is not resolved within such 60-day period, such dispute shall be settled exclusively by arbitration in the greater Boston, Massachusetts area, in accordance with the rules of the American Arbitration Association then in effect. Judgment may be entered on the

arbitrator's award in any court having jurisdiction. The Company shall, within three business days following delivery to the Company of the Executive Response, make to Executive those Potential Payments as to which there is no dispute between the Company and Executive regarding whether they should be made (except for any such Potential Payments which are not due to be made until after such date, which Potential Payments shall be made on the date on which they are due). The balance of the Potential Payments shall be made within three business days following the resolution of such dispute.

(v) The Contingent Compensation Payments to be treated as Eliminated Payments shall be determined by the Company by determining the "Contingent Compensation Payment Ratio" (as defined below) for each Contingent Compensation Payment and then reducing the Contingent Compensation Payments in order beginning with the Contingent Compensation Payment with the highest Contingent Compensation Payment Ratio. For Contingent Compensation Payments with the same Contingent Compensation Payment Ratio, such Contingent Compensation Payment shall be reduced based on the time of payment of such Contingent Compensation Payments with amounts having later payment dates being reduced first. For Contingent Compensation Payments with the same Contingent Compensation Payment Ratio and the same time of payment, such Contingent Compensation Payments shall be reduced on a pro rata basis (but not below zero) prior to reducing Contingent Compensation Payments with a lower Contingent Compensation Payment Ratio. The term "Contingent Compensation Payment Ratio" shall mean a fraction the numerator of which is the value of the applicable Contingent Compensation Payment that must be taken into account by Executive for purposes of Section 4999(a) of the Code, and the denominator of which is the actual amount to be received by Executive in respect of the applicable Contingent Compensation Payment. For example, in the case of an equity grant that is treated as contingent on the Change in Ownership or Control because the time at which the payment is made or the payment vests is accelerated, the denominator shall be determined by reference to the fair market value of the equity at the acceleration date, and not in accordance with the methodology for determining the value of accelerated payments set forth in Treasury Regulation Section 1.280G-1Q/A-24(b) or (c)).

(vi) The provisions of this Section 4(e) are intended to apply to any and all payments or benefits available to Executive under this Agreement or any other agreement or plan of the Company under which Executive receives Contingent Compensation Payments.

5. Employee Covenants.

(a) Confidential Information. Executive recognizes and acknowledges the competitive and proprietary aspects of the business of the Company, and that as a result of Executive's employment, Executive recognizes and acknowledges that he has had and will continue to have access to, and has been and will continue to be involved in the development of, Confidential Information (as defined below) of the Company. As used herein, "Confidential Information" shall mean and include trade secrets, knowledge and other confidential information of the Company, which Executive has acquired, no matter from whom or on what matter such knowledge or information may have been acquired, heretofore or hereafter, concerning the content and details of the business of the Company, and which is not known to the general public, including but not limited to: confidential and proprietary information supplied to

Executive with the legend "Confidential and Proprietary," or equivalent, the Company's marketing and customer support strategies, suppliers and customers, marketing and selling, business plans, licenses, the Company's financial information, including sales, costs, profits, prices, pricing methods, budgets and unpublished financial statements, the Company's internal organization, employee information obtained pursuant to Executive's duties and responsibilities, information regarding the skills and compensation of other employees of the Company obtained pursuant to Executive's duties and responsibilities and customer lists, the Company's technology, including products, discoveries, inventions, research, experimental and development efforts, clinical studies, processes, hardware/software design and maintenance tools, samples, media and/or molecular structures (and procedures and formulations for producing any such samples, media and/or molecular structures), formulas, methods, know-how and show-how, designs, prototypes, plans for research and new products, and all derivatives, improvements and enhancements of any of the above and information of third parties as to which the Company has an obligation of confidentiality.

(i) For as long as Executive is employed and at all times thereafter, Executive shall not, directly or indirectly, communicate, disclose or divulge to any person or entity, or use for Executive's own benefit or the benefit of any person (other than the Company), any Confidential Information, except as permitted in subparagraph (iii) below. Upon termination of Executive's employment, or at any other time at the request of the Company, Executive agrees to deliver promptly to the Company all Confidential Information, including, but not limited to, customer and supplier lists, files and records, in Executive's possession or under Executive's control. Executive further agrees that he will not make or retain any copies of any of the foregoing and will so represent to the Company upon termination of Executive's employment.

(ii) Executive shall disclose immediately to the Company any trade secrets or other Confidential Information conceived or developed by Executive at any time during Executive's employment. Executive hereby assigns and agrees to assign to the Company Executive's entire right, title and interest in and to all Confidential Information. Such assignment shall include, without limitation, the rights to obtain patent or copyright protection thereon in the United States and foreign countries. Executive agrees to provide all reasonable assistance to enable the Company to prepare and prosecute any application before any governmental agency for patent or copyright protection or any similar application with respect to any Confidential Information, at the expense of the Company. Executive further agrees to execute all documents and assignments and to make all oaths necessary to vest ownership of such intellectual property rights in the Company, as the Company may request. These obligations shall apply whether or not the subject thereof was conceived or developed at the suggestion of the Company, and whether or not developed during regular hours of work or while on the premises of the Company. The Company shall pay Executive at his then current reasonable consulting rate for any assistance it requests under this subsection (ii) other than the execution and delivery of documents, in the event that the Company is not paying Executive a salary or severance under this Agreement or compensation under any other agreement between the Company and Executive.

(iii) Except as set forth below, Executive shall at all times, both during and after termination of this Agreement by either Executive or the Company, maintain in confidence and shall not, without prior written consent of the Company, use, except in

the course of performance of Executive's duties for the Company or as required by legal process (provided that Executive will promptly notify the Company of such legal process except with respect to any confidential government investigation), disclose or give to others any Confidential Information. Executive agrees to abide by all Company policies and procedures pertaining to Confidential Information. Notwithstanding the foregoing, however, nothing in this Agreement or elsewhere prohibits Executive from communicating with government agencies about possible violations of federal, state, or local laws or otherwise providing information to government agencies, filing a complaint with government agencies, or participating in government agency investigations or proceedings. Executive is not required to notify the Company of any such communications; provided, however, that nothing herein authorizes the disclosure of information the Employee obtained through a communication that was subject to the attorney-client privilege. Further, notwithstanding Executive's confidentiality and nondisclosure obligations, Executive is hereby advised as follows pursuant to the Defend Trade Secrets Act: "An individual shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of a trade secret that (A) is made (i) in confidence to a Federal, State, or local government official, either directly or indirectly, or to an attorney; and (ii) solely for the purpose of reporting or investigating a suspected violation of law; or (B) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal. An individual who files a lawsuit for retaliation by an employer for reporting a suspected violation of law may disclose the trade secret to the attorney of the individual and use the trade secret information in the court proceeding, if the individual (A) files any document containing the trade secret under seal; and (B) does not disclose the trade secret, except pursuant to court order."

(b) Non-Competition and Non-Solicitation. Executive recognizes that the Company is engaged in a competitive business and that the Company has a legitimate interest in protecting its trade secrets, confidential business information, and customer, business development partner, licensee, supplier, and credit and/or financial relationships. Accordingly, in exchange for valuable consideration, including without limitation Executive's access to confidential business information and continued at-will employment, Executive agrees that, during the term hereof and for a period of twelve (12) months thereafter, Executive shall not:

(i) directly or indirectly, whether for himself or for any other person or entity, and whether as a proprietor, principal, shareholder, partner, agent, employee, consultant, independent contractor, or in any other capacity whatsoever, undertake or have any interest in (other than the passive ownership of publicly registered securities representing an ownership interest of less than 1%), engage in or assume any role involving directly or indirectly any business activity which is in competition with the products or services being developed, marketed, sold or otherwise provided by the Company or any other business in which the Company is engaged and for which Executive has rendered services while employed by the Company, or enter into any agreement to do any of the foregoing; or

(ii) initiate contact with (including without limitation phone calls, press releases and the sending or delivering of announcements), or in any manner solicit, directly or indirectly, any customers, business development partners, licensors, licensees, or creditors (including institutional lenders, bonding companies and trade creditors) of the Company in an attempt to induce or motivate them either to discontinue or modify their

then prevailing or future relationship with the Company or to transfer any of their business with the Company to any person or entity other than the Company; or

(iii) initiate contact with, or in any manner solicit, directly or indirectly, any supplier of goods, services or materials to the Company in an attempt to induce or motivate them either to discontinue or modify their then prevailing or future relationship with the Company or to supply the same or similar inventory, goods, services or materials (except generally available inventory, goods, services or materials) to any person or entity other than the Company; or

(iv) directly or indirectly recruit, solicit or otherwise induce or influence any employee or independent contractor of the Company to discontinue or modify his or her employment or engagement with the Company, or employ or contract with any such employee or contractor for the provision of services; *provided that* this subsection (iv) shall not prohibit Executive from hiring or engaging any person who responds to a general advertisement or solicitation, including but not limited to advertisements or solicitations through newspapers, trade publications, periodicals, websites, or efforts by any recruiting or employment agencies, so long as such general advertisement or solicitation is not targeted at or directed to the Company's employees or contractors.

(c) Definition of "Customer". The term "customer" or "customers" shall include any person or entity (a) that is a current customer of the Company, (b) that was a customer of the Company at any time during the preceding twenty-four (24) months or (c) to which the Company made a written presentation for the solicitation of business at any time during the preceding twenty-four (24) months (provided that Executive has knowledge, without investigation, of such solicitation).

(d) Reasonableness of Restrictions. Executive further recognizes and acknowledges that (i) the types of employment which are prohibited by this Section 5 are narrow and reasonable in relation to the skills which represent Executive's principal salable asset both to the Company and to Executive's other prospective employers, and (ii) the broad geographical scope of the provisions of this Section 5 is reasonable, legitimate and fair to Executive in light of the global nature of the Company's business, and in light of the limited restrictions on the type of employment prohibited herein compared to the types of employment for which Executive is qualified to earn Executive's livelihood.

(e) Remedies. Executive acknowledges that a breach of this Section 5 is likely to cause great and irreparable injury and damage, which cannot be reasonably or adequately compensated by money damages. Accordingly, Executive acknowledges that the remedies of injunction and specific performance shall be available in the event of such a breach, in addition to money damages, costs and attorneys' fees, and other legal or equitable remedies, and that the Company shall be entitled as a matter of course to an injunction pending trial, without the posting of bond or other security. Any period of restriction set forth in this Section 5 shall be extended for a period of time equal to the duration of any breach or violation hereof.

(f) Notification. Any person employing Executive or evidencing any intention to employ Executive may be notified as to the existence and provisions of this Agreement.

(g) Modification of Covenants; Enforceability. In the event that any provision of this Section 5 is held to be in any respect an unreasonable restriction, then the court so holding may modify the terms thereof, including the period of time during which it operates or the geographic area to which it applies, or effect any other change to the extent necessary to render this section enforceable, it being acknowledged by the parties that the representations and covenants set forth herein are of the essence of this Agreement.

(h) Subsidiaries. For purposes of Sections 5 and 6 of this Agreement, "Company" shall include all direct and indirect subsidiaries of the Company. An entity shall be deemed to be a subsidiary of the Company if the Company directly or indirectly owns or controls 50% or more of the equity interest in such entity.

6. Ownership of Ideas, Copyrights and Patents.

(a) Property of the Company. Executive agrees that all ideas, inventions, original works of authorship, developments, concepts, know-how, improvements or trade secrets, whether patentable, copyrightable or not, which Executive may conceive, reduce to practice or develop, alone or in conjunction with another, or others, whether during or out of regular business hours, and whether at the request or upon the suggestion of the Company, or otherwise, in the course of performing services for the Company in any capacity, whether heretofore or hereafter, (collectively, "the Inventions") are and shall be the sole and exclusive property of the Company, and that Executive shall not publish any of the Inventions without the prior written consent of the Company. Executive hereby assigns to the Company all of Executive's right, title and interest in and to all of the foregoing. Executive further represents and agrees that to the best of Executive's knowledge and belief none of the Inventions will violate or infringe upon any right, patent, copyright, trademark or right of privacy, or constitute libel or slander against or violate any other rights of any person, firm or corporation and that Executive will use his best efforts to prevent any such violation.

(b) Cooperation. At any time during or after the Term, Executive agrees that he will fully cooperate with the Company, its attorneys and agents in the preparation and filing of all papers and other documents as may be required to perfect the Company's rights in and to any of such Inventions, including, but not limited to, executing any lawful document (including, but not limited to, applications, assignments, oaths, declarations and affidavits) and joining in any proceeding to obtain letters patent, copyrights, trademarks or other legal rights of the United States and of any and all other countries on such Inventions, provided that any patent or other legal right so issued to Executive, personally, shall be assigned by Executive to the Company without charge by Executive. Executive further, in the event that Executive does not immediately comply with any request by the Company to obtain Executive's signature on documents necessary to vest such intellectual property rights in the Company, designates the Company as his agent for, and grants to the Company a power of attorney with full power of substitution, which power of attorney shall be deemed coupled with an interest, for the purpose of executing such documents as are necessary to effect the foregoing assignments from Executive to the Company. Company will bear the reasonable expenses which it causes to be incurred in Executive's assisting and cooperating hereunder, including compensating Executive for his time at his then current reasonable consulting rate in the event that the Company is not at the time of such assistance or cooperation paying Executive a salary or severance under this Agreement or compensation under any other agreement between the Company and Executive. Executive waives all claims to moral rights in any Inventions.

7. Disclosure to Future Employers. The Company may provide in its discretion, a copy of the covenants contained in Sections 5 and 6 of this Agreement to any business or enterprise which Executive may directly, or indirectly, own, manage, operate, finance, join, control or in which Executive participates in the ownership, management, operation, financing, or control, or with which Executive may be connected as an officer, director, employee, partner, principal, agent, representative, consultant or otherwise.

8. Records. Upon termination of Executive's relationship with the Company, Executive shall deliver to the Company any property of the Company which may be in Executive's possession including products, materials, memoranda, notes, records, reports, or other documents or photocopies of the same.

9. Insurance. The Company, in its sole discretion, may apply for and procure in its own name (whether or not for its own benefit) policies of insurance insuring Executive's life. Executive agrees to submit to reasonable medical or other examinations and to execute and deliver any applications or other instruments in writing that are reasonably necessary to effectuate such insurance. No adverse employment actions may be based upon the results of any such exam or the failure by the Company to obtain such insurance.

10. No Conflicting Agreements. Executive hereby represents and warrants that Executive has no commitments or obligations inconsistent with this Agreement.

11. Conditions to Employment. Notwithstanding anything to the contrary contained herein, this Agreement and Executive's employment hereunder is subject to and conditioned on satisfactory background checks, and Executive's provision of proof of his right to work in the United States.

12. General.

(a) Notices. All notices, requests, consents and other communications hereunder shall be in writing, shall be addressed to the receiving party's address as follows:

If to the Company: Ocular Therapeutix, Inc.
36 Crosby Drive, Suite 101
Bedford, MA 01730
USA
Attention: Chief Executive Officer
Telephone: (781) 357-4000

With an email copy to: AMattessich@ocutx.com

If to Executive: Michael Goldstein
3 Hurlbut St., Cambridge, MA. 02138

With an email copy to: mhgold81@gmail.com

or to such other address as a party may designate by notice hereunder, and shall be either (i) delivered by hand, (ii) sent by overnight courier, or (iii) sent by registered or certified mail, return receipt requested, postage prepaid. All notices, requests, consents and other

communications hereunder shall be deemed to have been given either (i) if by hand, at the time of the delivery thereof to the receiving party at the address of such party set forth above, (ii) if sent by overnight courier, on the next business day following the day such notice is delivered to the courier service, or (iii) if sent by registered or certified mail, on the fifth (5th) business day following the day such mailing is made.

(b) Entire Agreement. This Agreement embodies the entire agreement and understanding between the parties hereto with respect to the subject matter hereof and supersedes all prior oral or written agreements and understandings relating to the subject matter hereof. No statement, representation, warranty, covenant or agreement of any kind not expressly set forth in this Agreement shall affect, or be used to interpret, change or restrict, the express terms and provisions of this Agreement.

(c) Modifications and Amendments. The terms and provisions of this Agreement may be modified or amended only by written agreement executed by the parties hereto.

(d) Waivers and Consents. The terms and provisions of this Agreement may be waived, or consent for the departure therefrom granted, only by written document executed by the party entitled to the benefits of such terms or provisions. No such waiver or consent shall be deemed to be or shall constitute a waiver or consent with respect to any other terms or provisions of this Agreement, whether or not similar. Each such waiver or consent shall be effective only in the specific instance and for the purpose for which it was given, and shall not constitute a continuing waiver or consent.

(e) Assignment. The Company shall assign its rights and obligations hereunder to any person or entity that succeeds to all or substantially all of the Company's business or that aspect of the Company's business in which Executive is principally involved. Executive may not assign Executive's rights and obligations under this Agreement without the prior written consent of the Company.

(f) Benefit. All statements, representations, warranties, covenants and agreements in this Agreement shall be binding on the parties hereto and shall inure to the benefit of the respective successors and permitted assigns of each party hereto. Nothing in this Agreement shall be construed to create any rights or obligations except among the parties hereto, and no person or entity shall be regarded as a third-party beneficiary of this Agreement.

(g) Governing Law. This Agreement and the rights and obligations of the parties hereunder shall be construed in accordance with and governed by the law of The Commonwealth of Massachusetts, without giving effect to the conflict of law principles thereof.

(h) Jurisdiction and Service of Process. Any legal action or proceeding with respect to this Agreement shall be brought in the courts of The Commonwealth of Massachusetts or of the United States of America for the District of Massachusetts. By execution and delivery of this Agreement, each of the parties hereto accepts for itself and in respect of its property, generally and unconditionally, the jurisdiction of the aforesaid courts. Each of the parties hereto irrevocably consents to the service of process of any of the aforementioned courts in any such action or proceeding by the mailing of copies thereof by certified mail, postage prepaid, to the

party at its address set forth in Section 12(a) hereof. THE PARTIES IRREVOCABLY WAIVE ANY RIGHT TO TRIAL BY JURY AS TO ALL CLAIMS HEREUNDER.

(i) Severability. The parties intend this Agreement to be enforced as written. However, (i) if any portion or provision of this Agreement shall to any extent be declared illegal or unenforceable by a duly authorized court having jurisdiction, then the remainder of this Agreement, or the application of such portion or provision in circumstances other than those as to which it is so declared illegal or unenforceable, shall not be affected thereby, and each portion and provision of this Agreement shall be valid and enforceable to the fullest extent permitted by law; and (ii) if any provision, or part thereof, is held to be unenforceable because of the duration of such provision or the geographic area covered thereby, the Company and Executive agrees that the court making such determination shall have the power to reduce the duration and/or geographic area of such provision, and/or to delete specific words and phrases ("blue-penciling"), and in its reduced or blue-penciled form such provision shall then be enforceable and shall be enforced.

(j) Headings and Captions; Interpretation. The headings and captions of the various subdivisions of this Agreement are for convenience of reference only and shall in no way modify, or affect the meaning or construction of any of the terms or provisions hereof. The provisions of the following Sections of this Agreement are in addition to, and do not limit, each other: Sections 6 and 5(a); Sections 7 and 5(g); Sections 12(k) and 5(f); and Sections 12(l) and 12(d).

(k) Injunctive Relief. Executive hereby expressly acknowledges that any breach or threatened breach of any of the terms and/or conditions set forth in Section 5 or 6 of this Agreement is likely to result in substantial, continuing and irreparable injury to the Company. Therefore, Executive hereby agrees that, in addition to any other remedy that may be available to the Company, the Company shall be entitled to injunctive or other equitable relief by a court of appropriate jurisdiction.

(l) No Waiver of Rights, Powers and Remedies. No failure or delay by a party hereto in exercising any right, power or remedy under this Agreement, and no course of dealing between the parties hereto, shall operate as a waiver of any such right, power or remedy of the party. No single or partial exercise of any right, power or remedy under this Agreement by a party hereto, nor any abandonment or discontinuance of steps to enforce any such right, power or remedy, shall preclude such party from any other or further exercise thereof or the exercise of any other right, power or remedy hereunder. The election of any remedy by a party hereto shall not constitute a waiver of the right of such party to pursue other available remedies. No notice to or demand on a party not expressly required under this Agreement shall entitle the party receiving such notice or demand to any other or further notice or demand in similar or other circumstances or constitute a waiver of the rights of the party giving such notice or demand to any other or further action in any circumstances without such notice or demand.

(m) Counterparts. This Agreement may be executed in one or more counterparts, and by different parties hereto on separate counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

(n) Survival. The provisions of Sections 4, 5, 6, 7, 8, and 12 shall survive the termination of this Agreement and Executive's employment hereunder in accordance with their terms.

[*Remainder of Page Intentionally Left Blank*]

IN WITNESS THEREOF, the parties hereto have executed this Agreement as of the day and year first above written.

Ocular Therapeutix, Inc.

/s/ Antony Mattessich
Name: Antony Mattessich
Title: President and Chief Executive Officer

Agreed and Accepted

/s/ Michael Goldstein
Michael Goldstein

Exhibit 10.31

EMPLOYMENT AGREEMENT

This EMPLOYMENT AGREEMENT (the "Agreement") is made as of January 5, 2018 (the "Effective Date"), by and between Ocular Therapeutix, Inc., a Delaware corporation (the "Company"), and Kevin Hanley ("Executive"). In consideration of the mutual covenants contained in this Agreement, the Company and Executive agree as follows:

1. Employment. The Company agrees to employ Executive and Executive agrees to be employed by the Company on the terms and conditions set forth in this Agreement.

(a) Capacity. Executive shall serve the Company as Senior Vice President, Technical Operations reporting to the Company's Chief Executive Officer (the "CEO"). During the Term (as defined below) of Executive's employment with the Company, Executive shall, subject to the direction of the CEO, have the responsibilities, duties and authority commensurate with the position of Senior Vice President, Technical Operations and shall perform such other duties as may from time to time be assigned to him by the Company. The Company may change Executive's position, duties, and work location as it deems necessary.

(b) Devotion of Duties; Representations. During the Term of Executive's employment with the Company, Executive shall devote 100% of his best efforts and full business time and energies to the business and affairs of the Company, and shall endeavor to perform the duties and services contemplated hereunder to the reasonable satisfaction of the Company. During the Term of Executive's employment with the Company, Executive shall not, without the prior written approval of the Company (by action of the Company's Board of Directors (the "Board")), undertake any other employment from any person or entity or serve as a director of any other company; provided, however, that (i) the Company will entertain requests as to such other employment or directorships in good faith and (ii) Executive will be eligible to participate in any policy relating to outside activities that is applicable to the senior executives of the Company and approved by the Board after the date hereof, and provided further that in no event may any business activity be undertaken if it would (x) be in violation of any provision of this Agreement or other agreement between Executive and the Company, (y) interfere with the performance of Executive's duties for the Company, or (z) present a conflict of interest with the Company's business interests.

2. Term of Employment.

(a) Executive's employment hereunder shall begin on the Effective Date. Executive's employment hereunder shall be terminated upon the first to occur of the following:

(i) Immediately upon Executive's death;

(ii) By the Company, by written notice to Executive effective as of the date of such notice (or on such other date as specified in such notice):

(A) Following the Disability of Executive. "Disability" means that Executive (i) is unable to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment which can be expected to result in death or can be expected to last for a continuous period of

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

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

(C) Subject to Section 4 hereof, without Cause;

(iii) By Executive:

(A) At any time by written notice to the Company, effective thirty (30) days after the date of such notice; or

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

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

(b) Definition of "Cause". For purposes of this Agreement, "Cause" shall, pursuant to the reasonable good faith determination by the Company as documented in writing, include: (i) the willful and continued failure by Executive to substantially perform Executive's material duties or responsibilities under this Agreement (other than such a failure as a result of Disability); (ii) any action or omission by Executive involving willful misconduct or gross negligence with regard to the Company, which has a detrimental effect on the Company; (iii) Executive's conviction of a felony, either in connection with the performance of Executive's obligations to the Company or which otherwise shall adversely affect Executive's ability to perform such obligations or shall materially adversely affect the business activities, reputation, goodwill or image of the Company; (iv) the material breach of a fiduciary duty to the Company; or (v) the material breach by Executive of any of the provisions of this Agreement, provided that any breach of Executive's obligations with respect to Sections 5 or 6 of this Agreement, subject to the cure provision in the next sentence, shall be deemed "material." In respect of the events described in clauses (i) and (v) above, the Company shall give Executive notice of the failure of performance or breach, reasonable as to time, place and manner in the circumstances, and a 30-day opportunity to cure, provided that such failure of performance or breach is reasonably amenable to cure as determined by the Company in its sole discretion.

(c) Definition of "Good Reason". For purposes of this Agreement, a "Good Reason" shall mean any of the following, unless (i) the basis for such Good Reason is cured within

a reasonable period of time (determined in the light of the cure appropriate to the basis of such Good Reason, but in no event less than thirty (30) nor more than ninety (90) days) after the Company receives written notice (which must be received from Executive within ninety (90) days of the initial existence of the condition giving rise to such Good Reason) specifying the basis for such Good Reason or (ii) Executive has consented to the condition that would otherwise be a basis for Good Reason:

(i) A change in the principal location at which Executive provides services to the Company to a location more than fifty (50) miles from such principal location (which change, the Company has reasonably determined as of the date hereof, would constitute a material change in the geographic location at which Executive provides services to the Company), provided that such a relocation shall not be deemed to occur under circumstances where Executive's responsibilities require him to work at a location other than the corporate headquarters for a reasonable period of time;

(ii) A material adverse change by the Company in Executive's duties, authority or responsibilities which causes Executive's position with the Company to become of materially less responsibility or authority than Executive's position immediately following the Effective Date;

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

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

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

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

or restructuring beneficially own, directly or indirectly, more than 50% of the then-outstanding shares of common stock and the combined voting power of the then-outstanding securities entitled to vote generally in the election of directors, respectively, of the resulting or acquiring corporation in substantially the same proportions as their ownership of the Company's outstanding shares immediately prior to the merger, consolidation, reorganization or restructuring. Notwithstanding the foregoing, for any payments or benefits hereunder (including pursuant to Section 4(b)(iii) hereof) or pursuant to any other agreement between the Company and Executive, in either case that are subject to Section 409A, the Corporate Change must constitute a "change in control event" within the meaning of Treasury Regulation Section 1.409A-3(i)(5)(i).

3. Compensation.

(a) Base Salary. Executive's minimum base salary during the Term shall be at the rate of $335,000 per year. Executive's base salary shall be payable in substantially equal installments in accordance with the Company's payroll practices as in effect from time to time, less any amounts required to be withheld under applicable law. The base salary will be subject to adjustment from time to time in the sole discretion of the Company; provided that, the Company covenants that (A) during the first twelve months of Executive's employment, it shall not reduce Executive's base salary and (B) following such twelve month period, it shall not reduce the base salary below the base salary then in effect immediately prior to the reduction unless (i) Executive consents to such reduction, or (ii) the reduction is in connection with a general reduction of not more than 20% in compensation of senior executives of the Company generally that occurs prior to the effective date of any Corporate Change.

(b) Bonus. In addition to the base salary, the Company may pay Executive an annual bonus (the "Bonus") as determined by the Board, solely in its discretion (it being understood that Executive's target annual bonus shall be 35% of Executive's base salary in effect for such year, but may be higher or lower in any year in the Board's discretion). The Board's decision to issue a Bonus to Executive in any particular year shall have no effect on the absolute discretion of the Board to grant or not to grant a Bonus in subsequent years. Executive must be an active employee of the Company on December 31 of any calendar year in order to be eligible for and to earn any Bonus for that year. Any Bonus for a particular year shall be paid or provided to Executive in a lump sum no later than March 15th of the calendar year following the calendar year in which the Bonus was earned. For the avoidance of doubt, Executive will first be eligible for the Bonus in 2018, and will not be eligible to receive or earn any Bonus for the 2017 calendar year.

(c) Stock Option Grant. Subject to approval by the Board, the Company will grant to Executive an option to purchase 125,000 shares of the Company's common stock (the "Option"). The Option is subject to adjustment for stock splits, combinations or other recapitalizations. The exercise price per share of the Option shall be equal to the last reported sale price per share of the common stock on the NASDAQ stock exchange on the effective date of grant of the Option approved by the Board. The Option shall be issued pursuant to the Company's 2014 Equity Incentive Plan, as it may be amended from time to time, and will be subject to all of the terms and conditions set forth in such plan and the Stock Option Agreement covering the Option.

(d) Vacation. Executive shall be entitled to take 20 days of paid vacation during each year of the Term to be taken at such time or times as shall be mutually convenient and consistent with his duties and obligations to the Company. The number of vacation days for which Executive is eligible shall accrue at the rate of 1.67 days per month. Vacation is at all times subject to the Company's Time-Off Policy, which the Company may change periodically in its sole discretion.

(e) Fringe Benefits. Executive shall be entitled to participate in any employee benefit plans that the Company makes available to its executives (including, without limitation, group life, disability, medical, dental and other insurance, retirement, pension, profit-sharing and similar plans) (collectively, the "Fringe Benefits"), provided that the Fringe Benefits shall not include any stock option or similar plans relating to the grant of equity securities of the Company. These benefits may be modified or changed from time to time at the sole discretion of the Company. Where a particular benefit is subject to a formal plan (for example, medical or life insurance), eligibility to participate in and receive any particular benefit is governed solely by the applicable plan document, and eligibility to participate in such plan(s) may be dependent upon, among other things, a physical examination.

(f) Reimbursement of Expenses. Executive shall be entitled to reimbursement for all ordinary and reasonable out-of-pocket business expenses that are reasonably incurred by him in furtherance of the Company's business in accordance with reasonable policies adopted from time to time by the Company for senior executives, subject to Section 4(d)(v).

4. Severance Compensation.

(a) In the event of any termination of Executive's employment for any reason, the Company shall pay Executive (or Executive's estate) such portions of Executive's base salary as have accrued prior to such termination and have not yet been paid, together with (i) amounts for accrued unused vacation days (as provided above), (ii) any amounts for expense reimbursement which have been properly incurred or the Company has become obligated to pay prior to termination and have not been paid as of the date of such termination and (iii) the amount of any Bonus previously granted to Executive by the Board but not yet paid, which amount shall not include any pro rata portion of any Bonus which would have been earned if such termination had not occurred (the "Accrued Obligations"). Such Accrued Obligations shall be paid as soon as possible after termination, and in any event in accordance with applicable law.

(b) In the event that Executive's employment hereunder is terminated (i) by Executive for a Good Reason or (ii) by the Company without Cause, the Company shall pay to Executive the Accrued Obligations. In addition, the Company shall pay to Executive the severance benefits set forth below for twelve (12) months, or for eighteen (18) months if such termination occurs during the twelve (12) month period following a Corporate Change (the "Protected Period"), following Executive's termination of employment (as applicable, the "Severance Period"). The receipt of any severance benefits provided in this Section shall be dependent upon Executive's execution and, to the extent applicable, nonrevocation of a standard separation and general release of claims agreement, substantially in the form attached hereto as Exhibit A (the "Release"), which Release must be signed and any applicable revocation period with respect thereto must have expired by the sixtieth (60^{th}) day following Executive's termination of employment. The severance benefits

shall be paid or commence, as applicable, on the first payroll period following the date the Release becomes effective (the "Payment Date"). Notwithstanding the foregoing, if the 60th day following Executive's termination occurs in the calendar year following the date on which Executive's employment terminates, then the Payment Date shall be no earlier than January 1 of such subsequent calendar year.

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

(ii) Only if Executive's employment is terminated (A) by Executive for a Good Reason or (B) by the Company without Cause, in each case during the Protected Period, the Company shall pay Executive an amount equal to one and one-half times his target annual bonus, described in Section 3(b) hereof, for the year in which the termination of employment occurs, which total amount shall be payable in a lump sum on the Payment Date.

(iii) Only if Executive's employment is terminated (A) by Executive for a Good Reason or (B) by the Company without Cause, in each case during the Protected Period, one hundred percent (100%) of Executive's outstanding unvested equity awards granted under the Company's equity and long-term incentive plan(s) prior to his termination shall vest immediately.

(iv) The Company shall continue to provide Executive and his then-enrolled eligible dependents with group health insurance and shall continue to pay the amount of the premium as in effect on the date of such termination for the Severance Period commencing on the effective date of such termination, subject to applicable law and the terms of the respective policies; provided that the Company's obligation to provide the benefits contemplated herein shall terminate upon Executive's becoming eligible for coverage under the medical benefits program of a subsequent employer. The foregoing shall not be construed to extend any period of continuation coverage (e.g., COBRA) required by Federal law.

(c) In the event that Executive's employment hereunder is terminated (i) by Executive for other than a Good Reason, or (ii) by the Company for Cause, or (iii) as a result of Executive's death or Disability, then the Company will pay to Executive the Accrued Obligations. The Company shall have no obligation to pay Executive (or Executive's estate) any other compensation following such termination except as provided in Section 4(a).

(d) Compliance with Section 409A. Subject to the provisions in this Section 4(d), any severance payments or benefits under this Agreement shall begin only upon the date of Executive's "separation from service" (determined as set forth below) which occurs on or after the date of termination of Executive's employment. The following rules shall apply with respect to the distribution of the severance payments and benefits, if any, to be provided to Executive under this Agreement:

(i) It is intended that each installment of the severance payments and benefits provided under this Agreement shall be treated as a separate "payment" for purposes of Section 409A. Neither the Company nor Executive shall have the right to accelerate or defer the delivery of any such payments or benefits except to the extent specifically permitted or required by Section 409A.

(ii) If, as of the date of Executive's "separation from service" from the Company, Executive is not a "specified employee" (within the meaning of Section 409A), then each installment of the severance payments and benefits shall be made on the dates and terms set forth in this Agreement.

(iii) If, as of the date of Executive's "separation from service" from the Company, Executive is a "specified employee" (within the meaning of Section 409A), then:

(A) Each installment of the severance payments and benefits due under this Agreement that, in accordance with the dates and terms set forth herein, will in all circumstances, regardless of when the separation from service occurs, be paid within the short-term deferral period (as defined under Section 409A) shall be treated as a short-term deferral within the meaning of Treasury Regulation Section 1.409A-1(b)(4) to the maximum extent permissible under Section 409A and such payments and benefits shall be paid or provided on the dates and terms set forth in this Agreement; and

(B) Each installment of the severance payments and benefits due this Agreement that is not described in Section 4(d)(iii)(A) above and that would, absent this subsection (B), be paid within the six-month period following Executive's "separation from service" from the Company shall not be paid until the date that is six months and one day after such separation from service (or, if earlier, Executive's death), with any such installments that are required to be delayed being accumulated during the six-month period and paid in a lump sum on the date that is six months and one day following Executive's separation from service and any subsequent installments, if any, being paid in accordance with the dates and terms set forth herein; provided, however, that the preceding provisions of this sentence shall not apply to any installment of severance payments and benefits if and to the maximum extent that such installment is deemed to be paid under a separation pay plan that does not provide for a deferral of compensation by reason of the application of Treasury Regulation 1.409A-1(b)(9)(iii) (relating to separation pay upon an involuntary separation from service). Any installments that qualify for the exception under Treasury Regulation Section 1.409A-1(b)(9)(iii) must be paid no later than the last day of Executive's second taxable year following the taxable year in which the separation from service occurs.

(iv) The determination of whether and when Executive's separation from service from the Company has occurred shall be made in a manner consistent with, and based on the presumptions set forth in, Treasury Regulation Section 1.409A-1(h). Solely for purposes of this Section 4(d)(iv), "Company" shall include all persons with

whom the Company would be considered a single employer under Section 414(b) and 414(c) of the Code.

(v) All reimbursements and in-kind benefits provided under this Agreement shall be made or provided in accordance with the requirements of Sections 409A to the extent that such reimbursements or in-kind benefits are subject to Section 409A, including, where applicable, the requirements that (i) any reimbursement is for expenses incurred during Executive's lifetime (or during a shorter period of time specified in this Agreement), (ii) the amount of expenses eligible for reimbursement during a calendar year may not affect the expenses eligible for reimbursement in any other calendar year, (iii) the reimbursement of an eligible expense will be made on or before the last day of the calendar year following the year in which the expense is incurred and (iv) the right to reimbursement is not subject to set off or liquidation or exchange for any other benefit.

(vi) Notwithstanding anything herein to the contrary, the Company shall have no liability to Executive or to any other person if the payments and benefits provided hereunder that are intended to be exempt from or compliant with Section 409A are not so exempt or compliant.

(e) Modified Section 280G Cutback.

(i) Notwithstanding any other provision of this Agreement, except as set forth in Section 4(e)(ii), in the event that the Company undergoes a "Change in Ownership or Control" (as defined below), the Company shall not be obligated to provide to Executive a portion of any "Contingent Compensation Payments" (as defined below) that Executive would otherwise be entitled to receive to the extent necessary to eliminate any "excess parachute payments" (as defined in Section 280G(b)(1) of the Code) for Executive. For purposes of this Section 4(e), the Contingent Compensation Payments so eliminated shall be referred to as the "Eliminated Payments" and the aggregate amount (determined in accordance with Treasury Regulation Section 1.280G-1, Q/A-30 or any successor provision) of the Contingent Compensation Payments so eliminated shall be referred to as the "Eliminated Amount."

(ii) Notwithstanding the provisions of Section 4(e)(i), no such reduction in Contingent Compensation Payments shall be made if (1) the Eliminated Amount (computed without regard to this sentence) exceeds (2) 100% of the aggregate present value (determined in accordance with Treasury Regulation Section 1.280G-1, Q/A-31 and Q/A-32 or any successor provisions) of the amount of any additional taxes that would be incurred by Executive if the Eliminated Payments (determined without regard to this sentence) were paid to him (including federal and state income taxes on the Eliminated Payments, the excise tax imposed by Section 4999 of the Code payable with respect to all of the Contingent Compensation Payments in excess of Executive's "base amount" (as defined in Section 280G(b)(3) of the Code), and any withholding taxes). The override of such reduction in Contingent Compensation Payments pursuant to this Section 4(e)(ii) shall be referred to as a "Section 4(e)(ii) Override." For purpose of this paragraph, if any federal or state income taxes would be attributable to the receipt of any

Eliminated Payment, the amount of such taxes shall be computed by multiplying the amount of the Eliminated Payment by the maximum combined federal and state income tax rate provided by law.

(iii) For purposes of this Section 4(e) the following terms shall have the following respective meanings:

(1) "Change in Ownership or Control" shall mean a change in the ownership or effective control of the Company or in the ownership of a substantial portion of the assets of the Company determined in accordance with Section 280G(b)(2) of the Code.

(2) "Contingent Compensation Payment" shall mean any payment (or benefit) in the nature of compensation that is made or made available (under this Agreement or otherwise) to a "disqualified individual" (as defined in Section 280G(c) of the Code) and that is contingent (within the meaning of Section 280G(b)(2)(A)(i) of the Code) on a Change in Ownership or Control of the Company.

(iv) Any payments or other benefits otherwise due to Executive following a Change in Ownership or Control that could reasonably be characterized (as determined by the Company) as Contingent Compensation Payments (the "Potential Payments") shall not be made until the dates provided for in this Section 4(e)(iv). Within 30 days after each date on which Executive first becomes entitled to receive (whether or not then due) a Contingent Compensation Payment relating to such Change in Ownership or Control, the Company shall determine and notify Executive (with reasonable detail regarding the basis for its determinations) (1) which Potential Payments constitute Contingent Compensation Payments, (2) the Eliminated Amount and (3) whether the Section 4(e)(ii) Override is applicable. Within 30 days after delivery of such notice to Executive, Executive shall deliver a response to the Company (the "Executive Response") stating either (A) that he agrees with the Company's determination pursuant to the preceding sentence or (B) that he disagrees with such determination, in which case he shall set forth (x) which Potential Payments should be characterized as Contingent Compensation Payments, (y) the Eliminated Amount, and (z) whether the Section 4(e)(ii) Override is applicable. In the event that Executive fails to deliver an Executive Response on or before the required date, the Company's initial determination shall be final. If Executive states in the Executive Response that he agrees with the Company's determination, the Company shall make the Potential Payments to Executive within three business days following delivery to the Company of the Executive Response (except for any Potential Payments which are not due to be made until after such date, which Potential Payments shall be made on the date on which they are due). If Executive states in the Executive Response that he disagrees with the Company's determination, then, for a period of 60 days following delivery of the Executive Response, Executive and the Company shall use good faith efforts to resolve such dispute. If such dispute is not resolved within such 60-day period, such dispute shall be settled exclusively by arbitration in the greater Boston, Massachusetts area, in accordance with the rules of the American Arbitration Association then in effect. Judgment may be entered on the arbitrator's award in any court having jurisdiction. The Company shall, within three

business days following delivery to the Company of the Executive Response, make to Executive those Potential Payments as to which there is no dispute between the Company and Executive regarding whether they should be made (except for any such Potential Payments which are not due to be made until after such date, which Potential Payments shall be made on the date on which they are due). The balance of the Potential Payments shall be made within three business days following the resolution of such dispute.

(v) The Contingent Compensation Payments to be treated as Eliminated Payments shall be determined by the Company by determining the "Contingent Compensation Payment Ratio" (as defined below) for each Contingent Compensation Payment and then reducing the Contingent Compensation Payments in order beginning with the Contingent Compensation Payment with the highest Contingent Compensation Payment Ratio. For Contingent Compensation Payments with the same Contingent Compensation Payment Ratio, such Contingent Compensation Payment shall be reduced based on the time of payment of such Contingent Compensation Payments with amounts having later payment dates being reduced first. For Contingent Compensation Payments with the same Contingent Compensation Payment Ratio and the same time of payment, such Contingent Compensation Payments shall be reduced on a pro rata basis (but not below zero) prior to reducing Contingent Compensation Payments with a lower Contingent Compensation Payment Ratio. The term "Contingent Compensation Payment Ratio" shall mean a fraction the numerator of which is the value of the applicable Contingent Compensation Payment that must be taken into account by Executive for purposes of Section 4999(a) of the Code, and the denominator of which is the actual amount to be received by Executive in respect of the applicable Contingent Compensation Payment. For example, in the case of an equity grant that is treated as contingent on the Change in Ownership or Control because the time at which the payment is made or the payment vests is accelerated, the denominator shall be determined by reference to the fair market value of the equity at the acceleration date, and not in accordance with the methodology for determining the value of accelerated payments set forth in Treasury Regulation Section 1.280G-1Q/A-24(b) or (c)).

(vi) The provisions of this Section 4(e) are intended to apply to any and all payments or benefits available to Executive under this Agreement or any other agreement or plan of the Company under which Executive receives Contingent Compensation Payments.

5. Employee Covenants.

(a) Confidential Information. Executive recognizes and acknowledges the competitive and proprietary aspects of the business of the Company, and that as a result of Executive's employment, Executive recognizes and acknowledges that he has had and will continue to have access to, and has been and will continue to be involved in the development of, Confidential Information (as defined below) of the Company. As used herein, "Confidential Information" shall mean and include trade secrets, knowledge and other confidential information of the Company, which Executive has acquired, no matter from whom or on what matter such knowledge or information may have been acquired, heretofore or hereafter, concerning the content and details of the business of the Company, and which is not known to the general public, including but not limited to: confidential and proprietary information supplied to

Executive with the legend "Confidential and Proprietary," or equivalent, the Company's marketing and customer support strategies, suppliers and customers, marketing and selling, business plans, licenses, the Company's financial information, including sales, costs, profits, prices, pricing methods, budgets and unpublished financial statements, the Company's internal organization, employee information obtained pursuant to Executive's duties and responsibilities, information regarding the skills and compensation of other employees of the Company obtained pursuant to Executive's duties and responsibilities and customer lists, the Company's technology, including products, discoveries, inventions, research, experimental and development efforts, clinical studies, processes, hardware/software design and maintenance tools, samples, media and/or molecular structures (and procedures and formulations for producing any such samples, media and/or molecular structures), formulas, methods, know-how and show-how, designs, prototypes, plans for research and new products, and all derivatives, improvements and enhancements of any of the above and information of third parties as to which the Company has an obligation of confidentiality.

(i) For as long as Executive is employed and at all times thereafter, Executive shall not, directly or indirectly, communicate, disclose or divulge to any person or entity, or use for Executive's own benefit or the benefit of any person (other than the Company), any Confidential Information, except as permitted in subparagraph (iii) below. Upon termination of Executive's employment, or at any other time at the request of the Company, Executive agrees to deliver promptly to the Company all Confidential Information, including, but not limited to, customer and supplier lists, files and records, in Executive's possession or under Executive's control. Executive further agrees that he will not make or retain any copies of any of the foregoing and will so represent to the Company upon termination of Executive's employment.

(ii) Executive shall disclose immediately to the Company any trade secrets or other Confidential Information conceived or developed by Executive at any time during Executive's employment. Executive hereby assigns and agrees to assign to the Company Executive's entire right, title and interest in and to all Confidential Information. Such assignment shall include, without limitation, the rights to obtain patent or copyright protection thereon in the United States and foreign countries. Executive agrees to provide all reasonable assistance to enable the Company to prepare and prosecute any application before any governmental agency for patent or copyright protection or any similar application with respect to any Confidential Information. Executive further agrees to execute all documents and assignments and to make all oaths necessary to vest ownership of such intellectual property rights in the Company, as the Company may request. These obligations shall apply whether or not the subject thereof was conceived or developed at the suggestion of the Company, and whether or not developed during regular hours of work or while on the premises of the Company.

(iii) Except as set forth below, Executive shall at all times, both during and after termination of this Agreement by either Executive or the Company, maintain in confidence and shall not, without prior written consent of the Company, use, except in the course of performance of Executive's duties for the Company or as required by legal process (provided that Executive will promptly notify the Company of such legal process except with respect to any confidential government investigation), disclose or give to others any Confidential Information. In the event Executive is questioned by anyone not

employed by the Company or by an employee of or a consultant to the Company not authorized to receive such information, in regard to any such information or any other secret or confidential work of the Company, or concerning any fact or circumstance relating thereto, Executive will promptly notify the Company. Notwithstanding the foregoing, however, nothing in this Agreement or elsewhere prohibits Executive from communicating with government agencies about possible violations of federal, state, or local laws or otherwise providing information to government agencies, filing a complaint with government agencies, or participating in government agency investigations or proceedings. Executive is not required to notify the Company of any such communications; provided, however, that nothing herein authorizes the disclosure of information the Employee obtained through a communication that was subject to the attorney-client privilege. Further, notwithstanding Executive's confidentiality and nondisclosure obligations, Executive is hereby advised as follows pursuant to the Defend Trade Secrets Act: "An individual shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of a trade secret that (A) is made (i) in confidence to a Federal, State, or local government official, either directly or indirectly, or to an attorney; and (ii) solely for the purpose of reporting or investigating a suspected violation of law; or (B) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal. An individual who files a lawsuit for retaliation by an employer for reporting a suspected violation of law may disclose the trade secret to the attorney of the individual and use the trade secret information in the court proceeding, if the individual (A) files any document containing the trade secret under seal; and (B) does not disclose the trade secret, except pursuant to court order."

(b) Non-Competition and Non-Solicitation. Executive recognizes that the Company is engaged in a competitive business and that the Company has a legitimate interest in protecting its trade secrets, confidential business information, and customer, business development partner, licensee, supplier, and credit and/or financial relationships. Accordingly, in exchange for valuable consideration, including without limitation Executive's access to confidential business information and continued at-will employment, Executive agrees that, during the term hereof and for a period of twelve (12) months thereafter, Executive shall not:

(i) directly or indirectly, whether for himself or for any other person or entity, and whether as a proprietor, principal, shareholder, partner, agent, employee, consultant, independent contractor, or in any other capacity whatsoever, undertake or have any interest in (other than the passive ownership of publicly registered securities representing an ownership interest of less than 1%), engage in or assume any role involving directly or indirectly any business activity which is directly or indirectly in competition with the products or services being developed, marketed, sold or otherwise provided by the Company or any other business in which the Company is engaged and for which Executive has rendered services while employed by the Company, or enter into any agreement to do any of the foregoing; or

(ii) initiate contact with (including without limitation phone calls, press releases and the sending or delivering of announcements), or in any manner solicit, directly or indirectly, any customers, business development partners, licensors, licensees, or creditors (including institutional lenders, bonding companies and trade creditors) of the Company in an attempt to induce or motivate them either to discontinue or modify their

then prevailing or future relationship with the Company or to transfer any of their business with the Company to any person or entity other than the Company; or

(iii) initiate contact with, or in any manner solicit, directly or indirectly, any supplier of goods, services or materials to the Company in an attempt to induce or motivate them either to discontinue or modify their then prevailing or future relationship with the Company or to supply the same or similar inventory, goods, services or materials (except generally available inventory, goods, services or materials) to any person or entity other than the Company; or

(iv) directly or indirectly recruit, solicit or otherwise induce or influence any employee or independent contractor of the Company to discontinue or modify his or her employment or engagement with the Company, or employ or contract with any such employee or contractor for the provision of services.

(c) Definition of "Customer". The term "customer" or "customers" shall include any person or entity (a) that is a current customer of the Company, (b) that was a customer of the Company at any time during the preceding twenty-four (24) months or (c) to which the Company made a written presentation for the solicitation of business at any time during the preceding twenty-four (24) months.

(d) Reasonableness of Restrictions. Executive further recognizes and acknowledges that (i) the types of employment which are prohibited by this Section 5 are narrow and reasonable in relation to the skills which represent Executive's principal salable asset both to the Company and to Executive's other prospective employers, and (ii) the broad geographical scope of the provisions of this Section 5 is reasonable, legitimate and fair to Executive in light of the global nature of the Company's business, and in light of the limited restrictions on the type of employment prohibited herein compared to the types of employment for which Executive is qualified to earn Executive's livelihood.

(e) Remedies. Executive acknowledges that a breach of this Section 5 will cause great and irreparable injury and damage, which cannot be reasonably or adequately compensated by money damages. Accordingly, Executive acknowledges that the remedies of injunction and specific performance shall be available in the event of such a breach, in addition to money damages, costs and attorneys' fees, and other legal or equitable remedies, and that the Company shall be entitled as a matter of course to an injunction pending trial, without the posting of bond or other security. Any period of restriction set forth in this Section 5 shall be extended for a period of time equal to the duration of any breach or violation hereof.

(f) Notification. Any person employing Executive or evidencing any intention to employ Executive may be notified as to the existence and provisions of this Agreement.

(g) Modification of Covenants; Enforceability. In the event that any provision of this Section 5 is held to be in any respect an unreasonable restriction, then the court so holding may modify the terms thereof, including the period of time during which it operates or the geographic area to which it applies, or effect any other change to the extent necessary to render this section enforceable, it being acknowledged by the parties that the representations and covenants set forth herein are of the essence of this Agreement.

(h) Subsidiaries. For purposes of Sections 5 and 6 of this Agreement, "Company" shall include all direct and indirect subsidiaries of the Company. An entity shall be deemed to be a subsidiary of the Company if the Company directly or indirectly owns or controls 50% or more of the equity interest in such entity.

6. Ownership of Ideas, Copyrights and Patents.

(a) Property of the Company. Executive agrees that all ideas, inventions, original works of authorship, developments, concepts, know-how, improvements or trade secrets, whether patentable, copyrightable or not, which Executive may conceive, reduce to practice or develop, alone or in conjunction with another, or others, whether during or out of regular business hours, and whether at the request or upon the suggestion of the Company, or otherwise, in the course of performing services for the Company in any capacity, whether heretofore or hereafter, (collectively, "the Inventions") are and shall be the sole and exclusive property of the Company, and that Executive shall not publish any of the Inventions without the prior written consent of the Company. Executive hereby assigns to the Company all of Executive's right, title and interest in and to all of the foregoing. Executive further represents and agrees that to the best of Executive's knowledge and belief none of the Inventions will violate or infringe upon any right, patent, copyright, trademark or right of privacy, or constitute libel or slander against or violate any other rights of any person, firm or corporation and that Executive will use his best efforts to prevent any such violation.

(b) Cooperation. At any time during or after the Term, Executive agrees that he will fully cooperate with the Company, its attorneys and agents in the preparation and filing of all papers and other documents as may be required to perfect the Company's rights in and to any of such Inventions, including, but not limited to, executing any lawful document (including, but not limited to, applications, assignments, oaths, declarations and affidavits) and joining in any proceeding to obtain letters patent, copyrights, trademarks or other legal rights of the United States and of any and all other countries on such Inventions, provided that any patent or other legal right so issued to Executive, personally, shall be assigned by Executive to the Company without charge by Executive. Executive further designates the Company as his agent for, and grants to the Company a power of attorney with full power of substitution, which power of attorney shall be deemed coupled with an interest, for the purpose of effecting the foregoing assignments from Executive to the Company. Company will bear the reasonable expenses which it causes to be incurred in Executive's assisting and cooperating hereunder. Executive waives all claims to moral rights in any Inventions.

7. Disclosure to Future Employers. The Company may provide in its discretion, a copy of the covenants contained in Sections 5 and 6 of this Agreement to any business or enterprise which Executive may directly, or indirectly, own, manage, operate, finance, join, control or in which Executive participates in the ownership, management, operation, financing, or control, or with which Executive may be connected as an officer, director, employee, partner, principal, agent, representative, consultant or otherwise.

8. Records. Upon termination of Executive's relationship with the Company, Executive shall deliver to the Company any property of the Company which may be in Executive's possession including products, materials, memoranda, notes, records, reports, or other documents or photocopies of the same.

9. Insurance. The Company, in its sole discretion, may apply for and procure in its own name (whether or not for its own benefit) policies of insurance insuring Executive's life. Executive agrees to submit to reasonable medical or other examinations and to execute and deliver any applications or other instruments in writing that are reasonably necessary to effectuate such insurance. No adverse employment actions may be based upon the results of any such exam or the failure by the Company to obtain such insurance.

10. No Conflicting Agreements. Executive hereby represents and warrants that Executive has no commitments or obligations inconsistent with this Agreement.

11. Conditions to Employment. Notwithstanding anything to the contrary contained herein, this Agreement and Executive's employment hereunder is subject to and conditioned on satisfactory background and reference checks, and Executive's provision of proof of his right to work in the United States.

12. General.

(a) Notices. All notices, requests, consents and other communications hereunder shall be in writing, shall be addressed to the receiving party's address as follows:

If to the Company: Ocular Therapeutix, Inc.
15 Crosby Drive
Bedford, MA 01730
USA
Attention: Chief Executive Officer
Telephone: (781) 357-4000

With an email copy to: AMattessich@ocutx.com

If to Executive: Kevin Hanley
101 Christian Way, North Andover, MA 01845

or to such other address as a party may designate by notice hereunder, and shall be either (i) delivered by hand, (ii) sent by overnight courier, or (iii) sent by registered or certified mail, return receipt requested, postage prepaid. All notices, requests, consents and other communications hereunder shall be deemed to have been given either (i) if by hand, at the time of the delivery thereof to the receiving party at the address of such party set forth above, (ii) if sent by overnight courier, on the next business day following the day such notice is delivered to the courier service, or (iii) if sent by registered or certified mail, on the fifth (5th) business day following the day such mailing is made.

(b) Entire Agreement. This Agreement embodies the entire agreement and understanding between the parties hereto with respect to the subject matter hereof and supersedes all prior oral or written agreements and understandings relating to the subject matter hereof. No statement, representation, warranty, covenant or agreement of any kind not expressly set forth in this Agreement shall affect, or be used to interpret, change or restrict, the express terms and provisions of this Agreement.

(c) Modifications and Amendments. The terms and provisions of this Agreement may be modified or amended only by written agreement executed by the parties hereto.

(d) Waivers and Consents. The terms and provisions of this Agreement may be waived, or consent for the departure therefrom granted, only by written document executed by the party entitled to the benefits of such terms or provisions. No such waiver or consent shall be deemed to be or shall constitute a waiver or consent with respect to any other terms or provisions of this Agreement, whether or not similar. Each such waiver or consent shall be effective only in the specific instance and for the purpose for which it was given, and shall not constitute a continuing waiver or consent.

(e) Assignment. The Company shall assign its rights and obligations hereunder to any person or entity that succeeds to all or substantially all of the Company's business or that aspect of the Company's business in which Executive is principally involved. Executive may not assign Executive's rights and obligations under this Agreement without the prior written consent of the Company.

(f) Benefit. All statements, representations, warranties, covenants and agreements in this Agreement shall be binding on the parties hereto and shall inure to the benefit of the respective successors and permitted assigns of each party hereto. Nothing in this Agreement shall be construed to create any rights or obligations except among the parties hereto, and no person or entity shall be regarded as a third-party beneficiary of this Agreement.

(g) Governing Law. This Agreement and the rights and obligations of the parties hereunder shall be construed in accordance with and governed by the law of The Commonwealth of Massachusetts, without giving effect to the conflict of law principles thereof.

(h) Jurisdiction and Service of Process. Any legal action or proceeding with respect to this Agreement shall be brought in the courts of The Commonwealth of Massachusetts or of the United States of America for the District of Massachusetts. By execution and delivery of this Agreement, each of the parties hereto accepts for itself and in respect of its property, generally and unconditionally, the jurisdiction of the aforesaid courts. Each of the parties hereto irrevocably consents to the service of process of any of the aforementioned courts in any such action or proceeding by the mailing of copies thereof by certified mail, postage prepaid, to the party at its address set forth in Section 12(a) hereof. THE PARTIES IRREVOCABLY WAIVE ANY RIGHT TO TRIAL BY JURY AS TO ALL CLAIMS HEREUNDER.

(i) Severability. The parties intend this Agreement to be enforced as written. However, (i) if any portion or provision of this Agreement shall to any extent be declared illegal or unenforceable by a duly authorized court having jurisdiction, then the remainder of this Agreement, or the application of such portion or provision in circumstances other than those as to which it is so declared illegal or unenforceable, shall not be affected thereby, and each portion and provision of this Agreement shall be valid and enforceable to the fullest extent permitted by law; and (ii) if any provision, or part thereof, is held to be unenforceable because of the duration of such provision or the geographic area covered thereby, the Company and Executive agrees that the court making such determination shall have the power to reduce the duration and/or geographic area of such provision, and/or to delete specific words and phrases ("blue-

penciling"), and in its reduced or blue-penciled form such provision shall then be enforceable and shall be enforced.

(j) Headings and Captions; Interpretation. The headings and captions of the various subdivisions of this Agreement are for convenience of reference only and shall in no way modify, or affect the meaning or construction of any of the terms or provisions hereof. The provisions of the following Sections of this Agreement are in addition to, and do not limit, each other: Sections 6 and 5(a); Sections 7 and 5(g); Sections 12(k) and 5(f); and Sections 12(l) and 12(d).

(k) Injunctive Relief. Executive hereby expressly acknowledges that any breach or threatened breach of any of the terms and/or conditions set forth in Section 5 or 6 of this Agreement will result in substantial, continuing and irreparable injury to the Company. Therefore, Executive hereby agrees that, in addition to any other remedy that may be available to the Company, the Company shall be entitled to injunctive or other equitable relief by a court of appropriate jurisdiction.

(l) No Waiver of Rights, Powers and Remedies. No failure or delay by a party hereto in exercising any right, power or remedy under this Agreement, and no course of dealing between the parties hereto, shall operate as a waiver of any such right, power or remedy of the party. No single or partial exercise of any right, power or remedy under this Agreement by a party hereto, nor any abandonment or discontinuance of steps to enforce any such right, power or remedy, shall preclude such party from any other or further exercise thereof or the exercise of any other right, power or remedy hereunder. The election of any remedy by a party hereto shall not constitute a waiver of the right of such party to pursue other available remedies. No notice to or demand on a party not expressly required under this Agreement shall entitle the party receiving such notice or demand to any other or further notice or demand in similar or other circumstances or constitute a waiver of the rights of the party giving such notice or demand to any other or further action in any circumstances without such notice or demand.

(m) Counterparts. This Agreement may be executed in one or more counterparts, and by different parties hereto on separate counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

(n) Survival. The provisions of Sections 4, 5, 6, 7, 8, and 12 shall survive the termination of this Agreement and Executive's employment hereunder in accordance with their terms.

IN WITNESS THEREOF, the parties hereto have executed this Agreement as of the day and year first above written.

Ocular Therapeutix, Inc.

/s/ Antony Mattessich
Name: Antony Mattessich
Title: President and Chief Executive Officer

Agreed and Accepted

/s/ Kevin Hanley
Name: Kevin Hanley

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (No. 333-210777) and Form S-8 (Nos. 333-198240, 333-202886, 333-210059 and 333-216622) of Ocular Therapeutix, Inc. of our report dated March 8, 2018 relating to the financial statements, which appears in this Form 10-K.

/s/PricewaterhouseCoopers LLP
Boston, Massachusetts
March 8, 2018

Exhibit 31.1

CERTIFICATIONS

I, Antony Mattessich, certify that:

1. I have reviewed this Annual Report on Form 10-K of Ocular Therapeutix, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 8, 2018

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

Exhibit 31.2

CERTIFICATIONS

I, Donald Notman, certify that:

1. I have reviewed this Annual Report on Form 10-K of Ocular Therapeutix, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 8, 2018

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

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Ocular Therapeutix, Inc. (the "Company") for the period ended December 31, 2017 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 8, 2018

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

Exhibit 32.2

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Ocular Therapeutix, Inc. (the "Company") for the period ended December 31, 2017 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 8, 2018

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